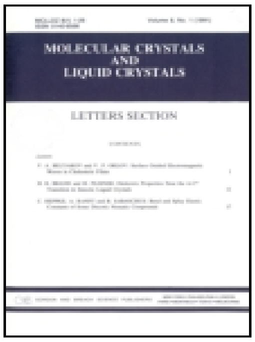
MOLECULAR CRYSTALS AND LIQUID CRYSTALS

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Synthesis, Characterization, and Crystal Structure of (E)-1-(4-(1-Isobutyl-1H-imidazo[4,5-c]quinolin-4-ylamino)phenyl)-3-phenylprop-2-en-1-one

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Synthesis, Characterization, and Crystal Structure of (*E*)-1-(4-(1-Isobutyl-1*H*-imidazo[4,5-*c*]quinolin-4-ylamino)phenyl)-3-phenylprop-2-en-1-one

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(E)-1-(4-(1-Isobutyl-1H-imidazo[4,5-c]quinolin-4-ylamino)phenyl)-3-phenylprop-2-en-1-one, $C_{29}H_{26}N_4O$, was synthesized and characterized by spectroscopy and elemental analysis. The crystal structure was determined from single crystal X-ray diffraction data. It crystallizes in the triclinic crystal system with the space group $P\bar{1}$, and unit cell parameters, $a = 9.667(2)$ Å, $b = 11.408(3)$ Å, $c = 12.286(3)$ Å, $\alpha = 116.7(1)°$, $\beta = 91.5(1)°$, $\gamma = 99.6(1)°$, $Z = 2$, CuKα = 1.5418 Å, and final R*1 and* wR*2 being 0.067 and 0.189, respectively. The molecular and crystal structures of the title molecule are stabilized by intramolecular interactions, N—H···N, C—H···N, and C—H···O, and intermolecular interaction, C—H···O.*

Keywords Characterization; crystal structure; imidazoquinoline; intermolecular interactions

1. Introduction

Chalcones, regarded as being the precursor of flavonoids and isoflavonoids, are abundant in edible plants. They consist of open-chain flavonoids in which the two aromatic rings are joined by a three-carbon α, β-unsaturated carbonyl system. Chalcones form the central core for a number of naturally occurring biologically active compounds. They exhibit tremendous potential to act as a pharmacological agent. Besides their various pharmacological activities, chalcones have been explored for different optical applications, including second harmonic generation materials in nonlinear optics, fluorescent probe for sensing different molecules [1]. Imidazoquinoline is a double cyclic organic molecule; its derivatives and compounds are synthetic, immunomodulatory drugs that act by binding toll-like receptors 7 and 8 (TLR7/TLR8) on dendritic cells [2, 3]. Imidazoquinoline amine compounds are now known

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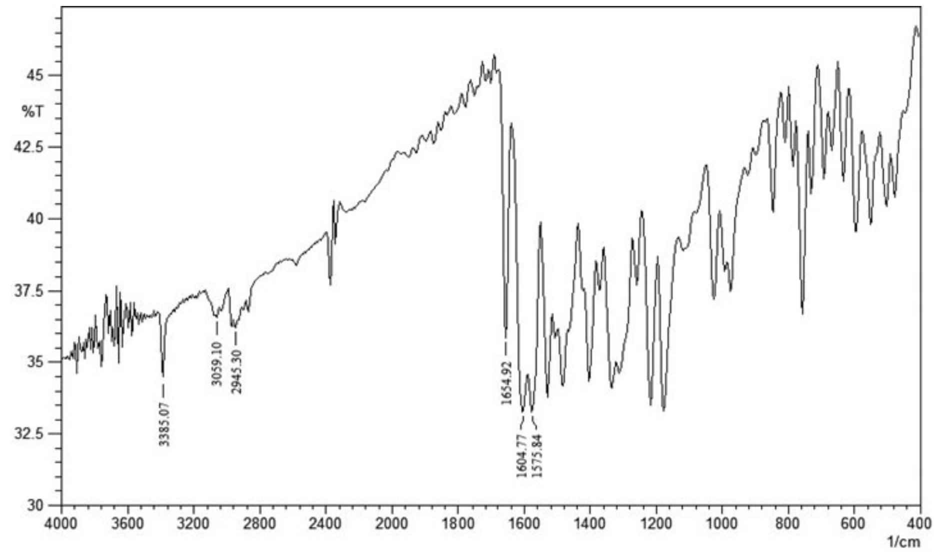


Figure 1. FT-IR spectrum of the title compound.

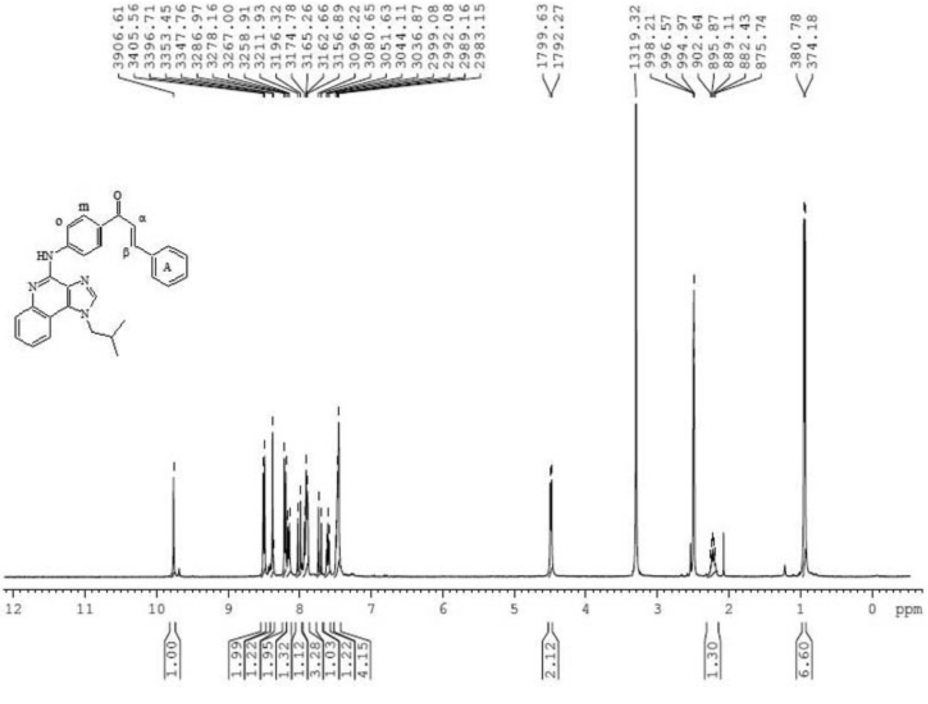


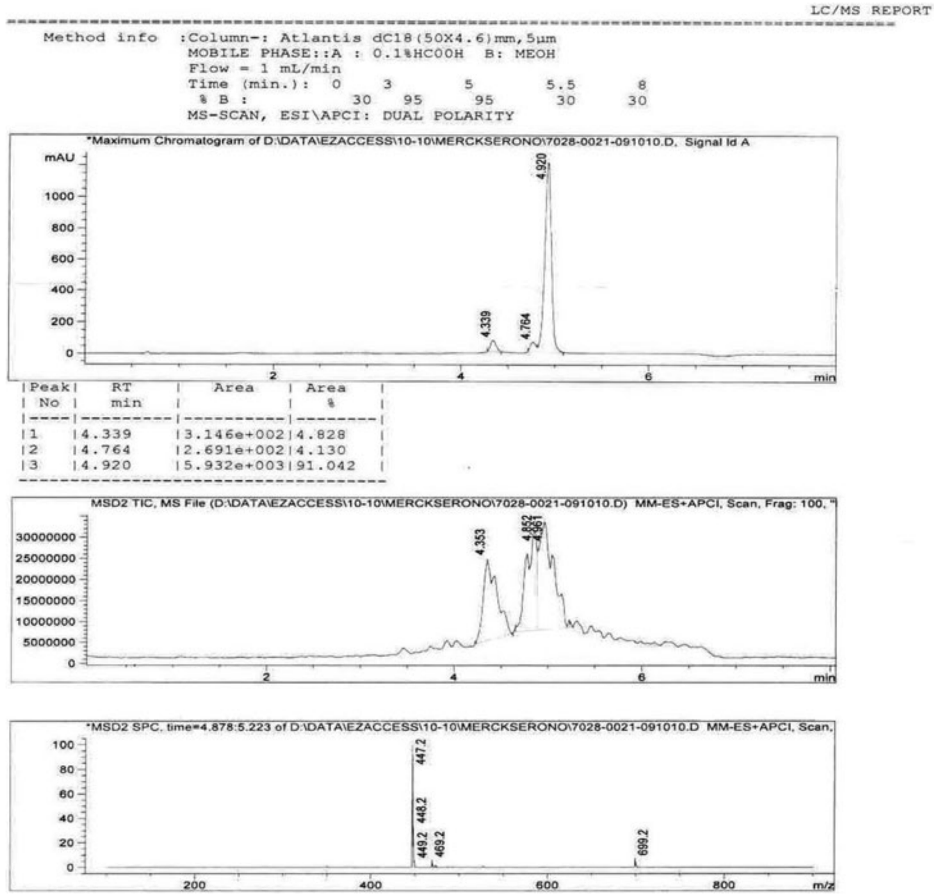
Figure 2. ^{1}H-NMR spectrum of the title compound.

Table 1. Elemental analysis of the compound, $C_{29}H_{26}N_4O$

Element	Experimental (%)	Calculated (%)
Carbon	78.06	78.00
Nitrogen	12.51	12.55
Hydrogen	5.89	5.87

to be the first small low molecular weight immune response modifiers that function through TLR receptors and have potent anti-viral, anti-tumor, non-xanthine adenosine antagonist properties. The biological activity associated with imiquimod has been attributed to its induction of interferon (IFN)-alpha [4].

The crucial interest of scientists in studying imidazoquinoline chalcone molecules is based on their vast diversity in applications. Prompted by these observations, it was contemplated to synthesize the title compound, (*E*)-1-(4-(1-Isobutyl-1*H*-imidazo[4,5-*c*]quinolin-4-ylamino)phenyl)-3-phenylprop-2-en-1-one, and characterize it by single crystal X-ray



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                                                              LC/MS REPORT
------------------------------------------------------------------------------
   Method info    :Column-: Atlantis dC18(50X4.6)mm,5µm
                   MOBILE PHASE::A : 0.1%HCOOH   B: MEOH
                   Flow = 1 mL/min
                   Time (min.):   0    3       5        5.5      8
                    % B :            30   95      95       30       30
                   MS-SCAN, ESI\APCI: DUAL POLARITY
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|Peak|   RT     |   Area    | Area   |
| No |   min    |           |   %    |
|----|----------|-----------|--------|
|1   |4.339     |3.146e+002|4.828    |
|2   |4.764     |2.691e+002|4.130    |
|3   |4.920     |5.932e+003|91.042   |
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Figure 3. LC-MS spectrum of the compound.

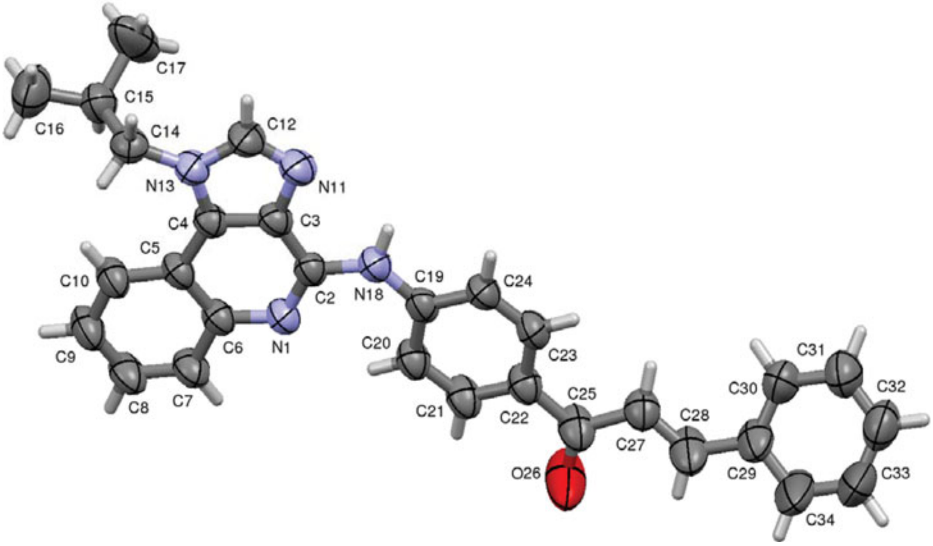


Figure 4. ORTEP of the molecule with numbering scheme for non-hydrogen atoms at 50% probability level.

diffraction, ^{1}H-Nuclear Magnetic Resonance (NMR) spectroscopy, Fourier transform-infrared spectroscopy (FT-IR), thermogravimetric analysis (TGA), UV-visible spectra, and elemental analysis.

2. Experimental

2.1. Materials and Methods

Melting point was determined in an open capillary tube, and was uncorrected. The purity of the compound was confirmed by thin layer chromatography using Merck silica gel

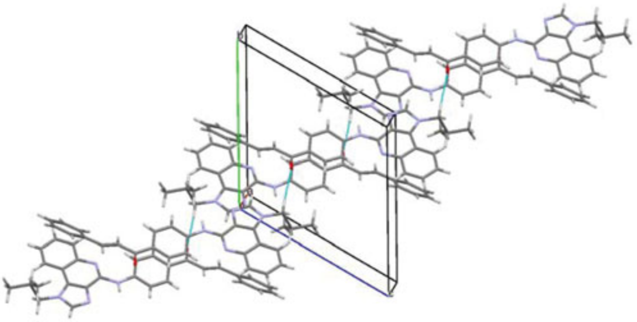


Figure 5. Packing of the molecules when viewed down along *a*-axis. The dotted lines represent C—H···O hydrogen bond interactions.

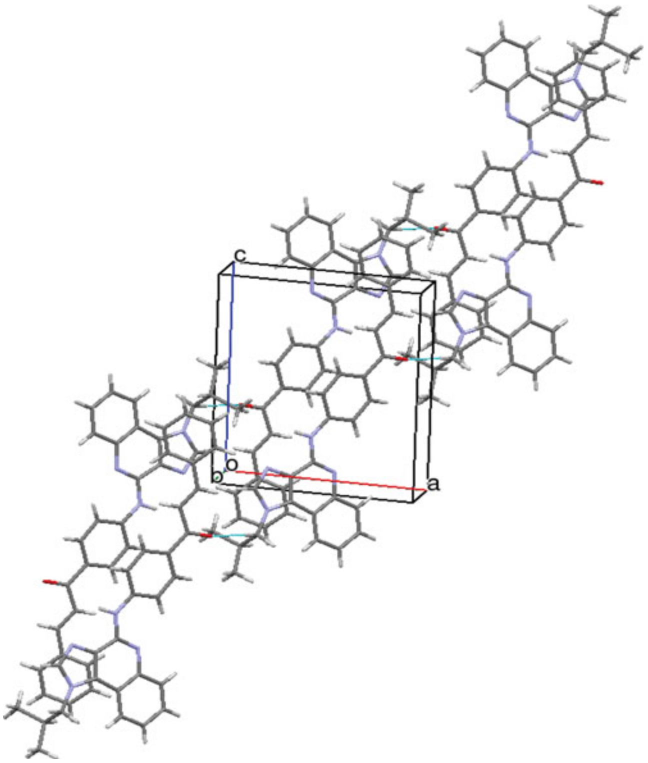


Figure 6. Packing of the molecules when viewed down along *b*-axis.

60 F_{254}-coated aluminium plates. Infrared (IR) spectrum was recorded on Shimadzu-FT-IR Infrared spectrometer in KBr (ν_{max} in cm^{-1}). ^{1}H-NMR (400 MHz) spectrum was recorded on a Bruker AMX-400 spectrometer, with 5-mm PABBO BB-1H TUBES, using DMSO-d_6 as a solvent and TMS as an internal standard (chemical shift in δ ppm). *Liquid*

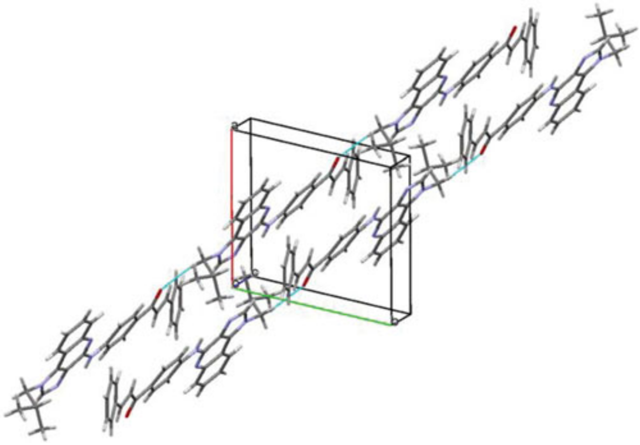


Figure 7. Packing of the molecules when viewed down along *c*-axis.

Table 2. Summary of crystal data and structure refinement

CCDC number	CCDC 974462
Empirical formula	$C_{29}H_{26}N_4O$
Formula weight	446.54 g mol^{-1}
Temperature	296 K
Wavelength	1.54178 Å
Crystal system, space group	Triclinic, $P\bar{1}$
Unit cell dimensions	$a = 9.667(2)$ Å $b = 11.408(3)$ Å $c = 12.286(3)$ Å $\alpha = 116.7(1)^\circ$ $\beta = 91.5(1)^\circ$ $\gamma = 99.6(1)^\circ$
Volume	1185.7(5) Å^3
Z, Calculated density	2, 1.251 Mg/m^3
Absorption coefficient	0.611 mm^{-1}
F_{000}	472
Crystal size	0.17 × 0.21 × 0.24 mm
Theta ranges for data collection	4.1 to 64.7°
Limiting indices	$-11 \leq h \leq 10, -10 \leq k \leq 13, -13 \leq l \leq 14$
Reflections collected/unique	14457/3871 ($R_{\text{int}} = 0.051$)
Absorption correction	Multi-scan, $T_{\text{min}} = 0.867$ and $T_{\text{max}} = 0.903$
Refinement method	Full-matrix least-square on F^2
Data/restraints/parameters	3871/0/310
Goodness-of-fit on F^2	1.07
Final R indices [$I > 2\text{sigma}(I)$]	$R1 = 0.067$, $wR2 = 0.189$
R indices (all data)	$R1 = 0.082$, $wR2 = 0.204$
Largest diff. peak and hole	0.35 and −0.33 e. Å^{-3}

chromatography–mass spectrum (LC-MS) was obtained using Agilent 1200 series LC and Micromass zQ spectrometer. Elemental analysis was carried out by using VARIO EL-III (Elementar Analysensysteme GmBH). All chemicals were purchased commercially and used without prior purification.

2.2. Synthesis of (E)-1-(4-(1-Isobutyl-1H-imidazo[4,5-c]quinolin-4-ylamino)phenyl)-3-phenylprop-2-en-1-one (2)

The method of synthesis of the compound 1-{4-[(1-Isobutyl-1*H*-imidazo[4,5-*c*]quinolin-4-yl)amino]phenyl}ethanone (**1**) has been reported earlier [5]. To the stirring solution of 1-{4-[(1-Isobutyl-1*H*-imidazo[4,5-*c*]quinolin-4-yl)amino]phenyl}ethanone (0.01 mol) and benzaldehyde (0.01 mol) in ethanol (30 mL) was added an aqueous solution of KOH (40%, 15 mL). The mixture was kept overnight at room temperature. It was poured into crushed ice and acidified with concentrated HCl. The product obtained was filtered, washed with water, and recrystallized from ethanol; the yield was 85%, showing melting point = 134–136°C (Scheme 1) [6].

Table 3. Selected bond lengths (Å) and bond angles (°)

N1—C2	1.312 (3)	C5—C6	1.423 (4)
N1—C6	1.383(3)	C6—C7	1.404(3)
C2—N18	1.379(3)	C7—C8	1.363(4)
C2—C3	1.416(4)	C8—C9	1.391(4)
C3—C4	1.378(3)	C9—C10	1.373(4)
C3—N11	1.383(3)	N11—C12	1.304(4)
C4—N13	1.379(3)	C12—N13	1.369(3)
C4—C5	1.430(3)	N13—C14	1.453(3)
C5—C10	1.408(4)	C14—C15	1.508(4)
C15—C17	1.514(5)		
C2—N1—C6	118.1(2)	N1—C6—C5	125.2(2)
N1—C2—N18	122.3(2)	C7—C6—C5	118.3(2)
N1—C2—C3	121.7(2)	C8—C7—C6	121.3(3)
N18—C2—C3	115.9(2)	C7—C8—C9	120.7(3)
C4—C3—N11	111.6(2)	C10—C9—C8	119.8(3)
C4—C3—C2	120.4(2)	C9—C10—C5	120.9(3)
N11—C3—C2	127.9(2)	C12—N11—C3	103.1(2)
C3—C4—N13	105.2(2)	N11—C12—N13	114.7(2)
C3—C4—C5	120.6(2)	C12—N13—C4	105.4(2)
N13—C4—C5	134.2(2)	C12—N13—C14	124.9(2)
C10—C5—C6	119.0(2)	C4—N13—C14	129.7(2)
C10—C5—C4	127.1(2)	N13—C14—C15	115.1(2)
C6—C5—C4	113.9(2)	C14—C15—C17	111.1(3)
N1—C6—C7	116.5(2)		

3. Results and Discussion

3.1. *FT-IR Spectral Analysis*

The IR spectral analysis was carried out to understand the chemical bonding, which provides useful information regarding the molecular structure of the compound. The FT-IR spectrum of the compound is shown in Figure 1. IR spectra showed strong absorption bands at 3385 and 3059 cm^{-1} due to NH and Ar CH groups. The carbonyl group of propenone moiety appeared as strong and sharp absorption band at 1654 cm^{-1}. Another strongly absorbed band at 1575 cm^{-1} was assigned to carbon–carbon double bond of α, β-unsaturated system.

3.2. *^{1}H Spectral Analysis*

The ^{1}H-NMR spectrum of the compound is shown in Figure 2. The ^{1}H-NMR spectrum showed doublet and septet resonating at δ 0.95 ppm ($J = 6.6$ Hz) and 2.25 ppm ($J = 6.7$ Hz), which was assigned to six methyl protons and one methine proton of isopropyl moiety. A doublet that appeared at δ 4.49 ppm ($J = 7.3$ Hz) was due to methylene protons. The trans-olefinic protons H_α and H_β as ortho-coupled doublets at δ 7.74 ppm and 8.02 ppm, have a coupling constant of $J = 15.6$ Hz between them, which is indicative of the *E*-configuration of chalcone. In addition, the aromatic protons appeared in the region δ 7.49–8.51 ppm. The

Table 4. Torsion angles (°)

C6—N1—C2—N18	179.2 (2)	C12—N13—C14—C15	96.7(3)
C6—N1—C2—C3	−0.9(4)	C4—N13—C14—C15	−83.6(3)
N1—C2—C3—C4	1.9(4)	N13—C14—C15—C17	−65.1(4)
N18—C2—C3—C4	−178.22)	N13—C14—C15—C16	172.9(3)
N1—C2—C3—N11	179.9(2)	N1—C2—N18—C19	−3.4(4)
N18—C2—C3—N11	−0.2(4)	C3—C2—N18—C19	176.7(2)
N11—C3—C4—N13	−0.4(3)	C2—N18—C19—C24	−171.2(2)
C2—C3—C4—N13	177.9(2)	C2—N18—C19—C20	8.4(4)
N11—C3—C4—C5	179.8(2)	N18—C19—C20—C21	−179.1(2)
C2—C3—C4—C5	−2.0(4)	C24—C19—C20—C21	0.6(4)
C3—C4—C5—C10	−178.2(2)	C19—C20—C21—C22	−0.9(4)
N13—C4—C5—C10	1.9(5)	C20—C21—C22—C23	0.5(4)
C3—C4—C5—C6	1.1(3)	C20—C21—C22—C25	0.5(4)
N13—C4—C5—C6	−178.8(2)	C21—C22—C23—C24	0.4(4)
C2—N1—C6—C7	179.0(2)	C25—C22—C23—C24	−177.8(3)
C2—N1—C6—C5	0.0(4)	C22—C23—C24—C19	−0.7(4)
C10—C5—C6—N1	179.2(2)	N18—C19—C24—C23	179.9(2)
C4—C5—C6—N1	−0.1(4)	C20—C19—C24—C23	0.3(4)
C10—C5—C6—C7	0.3(4)	C21—C22—C25—O26	−9.2(5)
C4—C5—C6—C7	−179.12)	C23—C22—C25—O26	168.9(3)
N1—C6—C7—C8	−179.2(3)	C21—C22—C25—C27	172.0(3)
C5—C6—C7—C8	−0.2(4)	C23—C22—C25—C27	−9.9(4)
C6—C7—C8—C9	0.1(5)	O26—C25—C27—C28	−12.9(5)
C7—C8—C9—C10	−0.1(5)	C22—C25—C27—C28	166.0(3)
C8—C9—C10—C5	0.2(5)	C25—C27—C28—C29	−178.7(4)
C6—C5—C10—C9	−0.3(4)	C27—C28—C29—C30	−14.1(7)
C4—C5—C10—C9	179.0(3)	C27—C28—C29—C34	161.5(6)
C4—C3—N11—C12	0.2(3)	C34—C29—C30—C31	3.3(7)
C2—C3—N11—C12	−177.8(3)	C28—C29—C30—C31	179.1(3)
C3—N11—C12—N13	0.0(3)	C29—C30—C31—C32	−3.8(6)
N11—C12—N13—C4	−0.2(3)	C30—C31—C32—C33	2.2(8)
N11—C12—N13—C14	179.6(2)	C31—C32—C33—C34	−0.4(1)
C3—C4—N13—C12	0.3(3)	C30—C29—C34—C33	−1.5(1)
C5—C4—N13—C12	−179.8(3)	C28—C29—C34—C33	−177.5(7)
C3—C4—N13—C14	−179.5(2)	C32—C33—C34—C29	0.2(2)
C5—C4—N13—C14	0.4(5)		

two singlets located at δ 8.38 ppm and 9.76 ppm indicated the presence of $CH = N$ group and one NH proton.

3.3. Elemental Analysis

The experimental and calculated percentages of C, H, and N are given in Table 1. The differences between experimental and calculated percentages of C, H, and N are very small

Table 5. Hydrogen bond geometry (Å, °)

D—H···*A*	d(*D*—H)	d(H···*A*)	d(*D*···*A*)	∠ *D*—H···*A*
C14—H14···O26$^{(i)}$	0.97	2.40	3.361(5)	170
N18—H18···N11	0.86	2.46	2.872(3)	110
C20—H20···N1	0.93	2.35	2.949(3)	122
C28—H28···O26	0.93	2.46	2.797(4)	101

Symmetry code: (i) $-1 + x$, $-1 + y$, $-1 + z$.

and within the experimental errors. This analysis confirms the formation of product in stoichiometric proportion.

3.4. LC-MS Analysis

The LC-MS spectrum of the compound is shown in Figure 3. The spectrum showed peak at 447, which corresponds to the molecular ion ($M^+ + 1$) peak of the title compound.

3.5. Single Crystal X-Ray Diffraction Method

A yellow block-shaped single crystal of dimensions 0.17 × 0.17 × 0.24 mm of the title compound was selected for data collection. X-ray intensity data were collected for the title compound at temperature 296 K on Bruker X8 Proteum X-ray diffractometer [7] with X-ray generator operating at 45 kV and 10 mA, using CuK$_\alpha$ radiation of wavelength $\lambda = 1.54178$ Å.

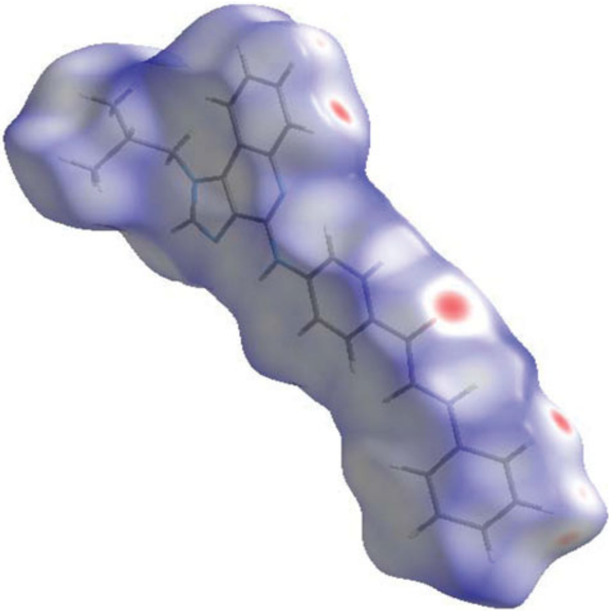


Figure 8. The Hirshfeld surface for visualizing the intercontacts of the molecule. Color scale between −0.050 au (blue) and 1.100 au (red).

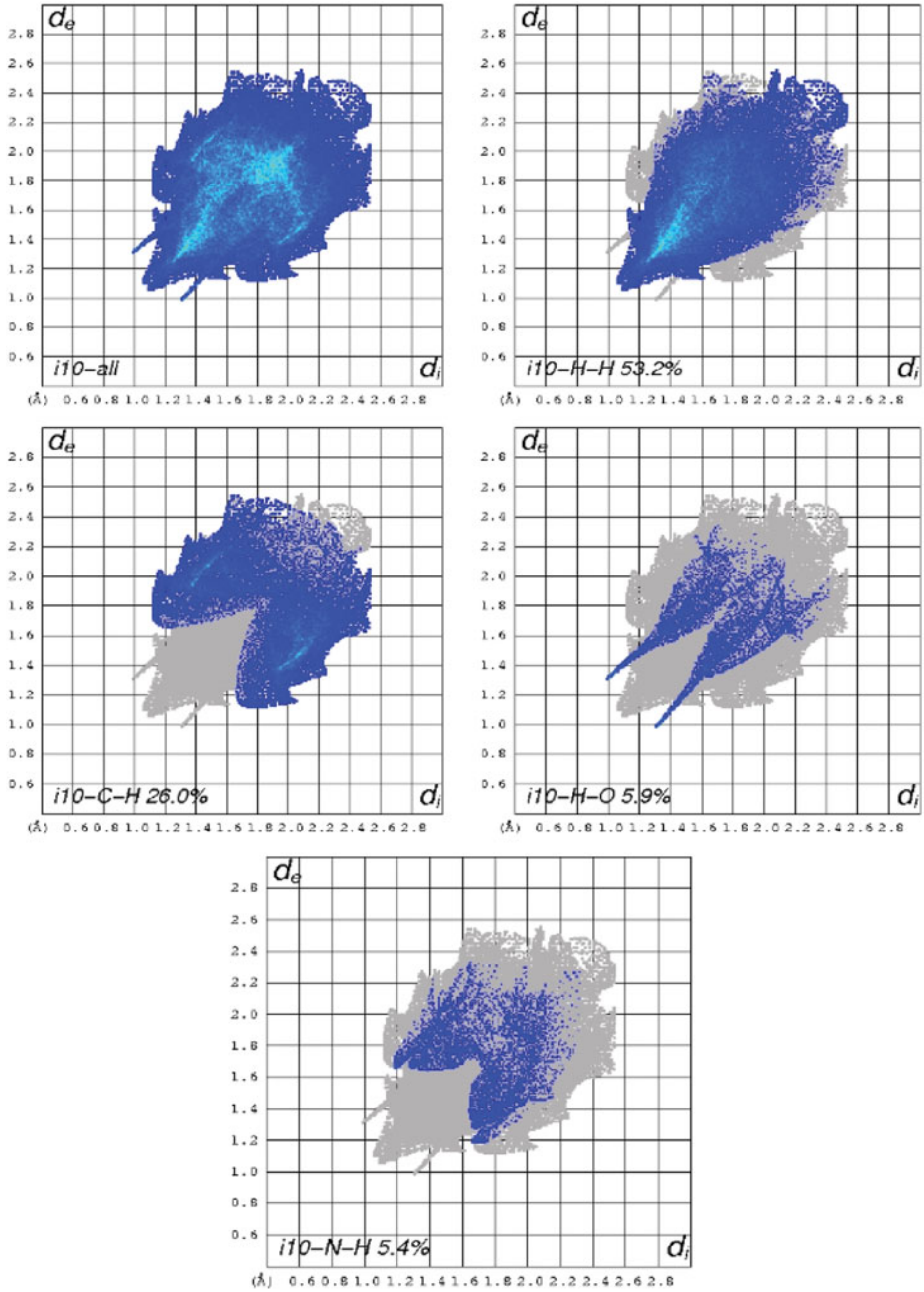


Figure 9. Finger print plots of the molecule.

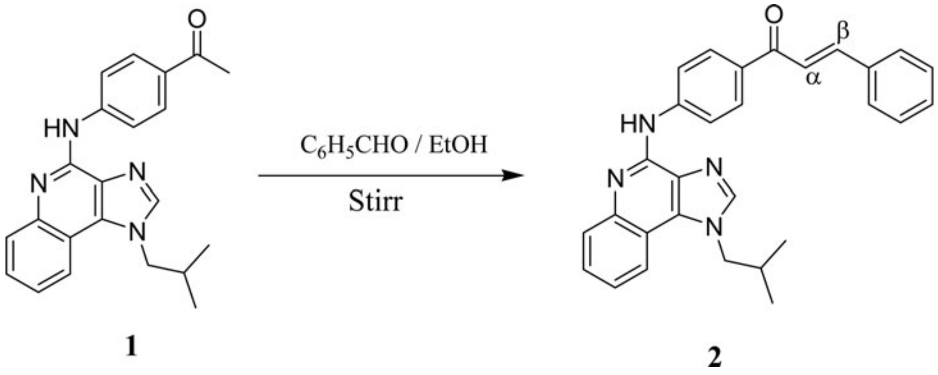
Data were collected with different settings of ϕ (0° and 90°), keeping the scan width of 0.5°, exposure time of 5 s and the sample to detector distance, 45.10 mm. A complete data set was processed using SAINT PLUS [8]. The structure was solved by direct methods using SHELXS and refined by full-matrix least squares method on F^2 using SHELXL [9]. The geometrical calculations were carried out using PLATON [10]. The molecular and packing diagrams were generated using the software MERCURY [11].

X-ray diffraction analysis revealed that the title compound is crystallized in the triclinic crystal system with the space group $P\bar{1}$ and unit cell parameters, $a = 9.667(2)$ Å, $b = 11.408(3)$ Å, $c = 12.286(3)$ Å, $\alpha = 116.7(1)°$, $\beta = 91.5(1)°$, $\gamma = 99.6(1)°$, and $V = 1185.7(5)$ Å^3. The ORTEP of the molecule with displacement ellipsoids drawn at 50% probability level is shown in Figure 4.

The packing of molecules when viewed along *a*, *b*, and *c*-axes are shown in Figures 5, 6 and 7 respectively. The crystal data and the details of the structure refinement are listed in Table 2. Bond lengths and bond angles are given in Table 3. Torsion angles and hydrogen bond geometry are given in Tables 4 and 5 respectively.

The imidazoquinoline ring N1/C2/C3/C4/C5/C6/C7/C8/C9/C10/N11/C12/N13 is planar as confirmed by the torsion angles of its segments. The plane of the phenyl ring C19/C20/C21/C22/C23/C24 forming a dihedral angle of 7.2(1)° with the plane of the imidazoquinoline ring N1/C2/C3/C4/C5/C6/C7/C8/C9/C10/N11/C12/N13 reflects that the plane of the phenyl ring is in an axial position with respect to the plane of the imidazoquinoline ring. The plane described by the phenyl ring C29/C30/C31/C32/C33/C34 not only bisects the imidazoquinoline plane as confirmed by the dihedral angle of 36.6(3)° but also the plane of the phenyl ring C19/C20/C21/C22/C23/C24 with a dihedral angle of 36.5(3)°. The bond lengths and bond angles of the title compound agree well with those reported earlier [12].

The structure exhibits by C—H···Cg_4 interaction; C14—H14B···Cg_4 (Cg_4 is the centroid of the ring C19/C20/C21/C22/C23/C24) with a C—Cg distance of 3.556(3) Å, H—Cg distance of 2.75 Å, C—H···Cg angle of 141°, and with a symmetry code $1-x$, $1-y$, $1-z$. The molecular structure is stabilized by the intramolecular interactions, N—H···N, C—H···N, and C—H···O, and in the crystal lattice, the molecules are stacked in layers and are connected by the C—H···O hydrogen bond interactions extended along (001) plane to stabilize the crystal structure, and are listed in Table 5.



Scheme 1. Synthesis of compound (*E*)-1-(4-(1-Isobutyl-1*H*-imidazo[4,5-*c*]quinolin-4-ylamino)phenyl)-3-phenylprop-2-en-1-one.

3.6. Hirshfeld Surface Analysis

In order to visualize the intercontacts in the molecular structure, the Hirshfeld surface analysis was carried out for the title molecule by the computational methods implemented in CRYSTAL EXPLORER [13]. The Hirshfeld surface and fingerprint plots are shown in Figures 8 and 9, respectively.

The Hirshfeld surface analysis shows that there exists intercontacts O···H and N···H, which show up as dark red spots that occur due to the hydrogen bond acceptors of C14—H14A···O26 and N18—H18···N11 interactions, and faint spots on the surface reflect C···H intercontacts. The intercontacts which contribute for the Hirshfeld surface are H···H (53%), C···H (26%), O···H (6%), and N···H (5%), which play a central role in the stabilization of molecules.

4. Conclusions

A new chalcone derivative (*E*)-1-(4-(1-Isobutyl-1*H*-imidazo[4,5-*c*]quinolin-4-ylamino)phenyl)-3-phenylprop-2-en-1-one has been synthesized using the Claisen–Schmidt condensation reaction method. The title compound was characterized using FT-IR, NMR, and UV-visible spectra, and TGA was carried out to study the thermal behavior of the crystal. The elemental analysis confirms the formation of the compound in a stoichiometric ratio. Single crystal is grown by the slow evaporation method using ethanol as a solvent. Finally, the structure of the compound is confirmed using the single crystal X-ray diffraction method. Spectral data show that the material may be useful for optoelectronic applications.

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