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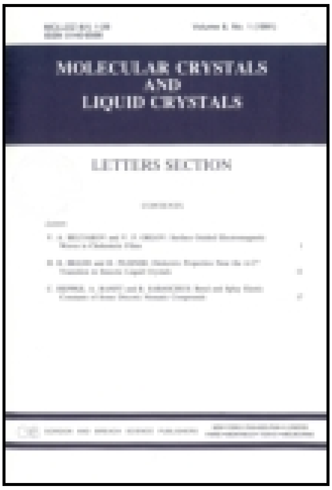

Molecular Crystals and Liquid Crystals
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gmcl20

Synthesis Characterization and Crystal Structure of 2-(3,4,5-trimethoxyphenyl)-1-(4-fluorophenyl)-4,5-diphenyl-1H-imidazole

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Published online: 27 May 2014.

To cite this article: S. Viveka, M. Prabhuswamy, Dinesha, N. K. Lokanath & G. K. Nagaraja (2014) Synthesis Characterization and Crystal Structure of 2-(3,4,5-trimethoxyphenyl)-1-(4-fluorophenyl)-4,5-diphenyl-1H-imidazole, Molecular Crystals and Liquid Crystals, 593:1, 261-270, DOI: 10.1080/15421406.2013.875761

To link to this article: http://dx.doi.org/10.1080/15421406.2013.875761

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Mol. Cryst. Liq. Cryst., Vol. 593: pp. 261–270, 2014
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ISSN: 1542-1406 print/1563-5287 online
DOI: 10.1080/15421406.2013.875761

Synthesis Characterization and Crystal Structure of 2-(3,4,5-trimethoxyphenyl)-1-(4-fluorophenyl)-4,5-diphenyl-1*H*-imidazole

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The title compound, $C_{30}H_{25}FN_2O_3$, was prepared from the four-component one-pot condensation reaction and the product crystallized using dimethylformamide. The structure of the compound was established by elemental analysis, Fourier transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA), UV-Visible, and single-crystal X-ray diffraction. The compound crystallizes in the triclinic crystal system with the space group $P\bar{1}$, with unit cell parameters $a = 10.286(2)$ Å, $b = 11.795(2)$ Å, $c = 21.331(4)$ Å, $\alpha = 100.270(3)^\circ$, $\beta = 90.093(3)^\circ$, $\gamma = 90.062(3)^\circ$, and $Z = 4$. The crystal and molecular structure of the title molecule is stabilized by intra-molecular interactions of types C–H···N and C–H···O.

Keywords Crystallization; crystal structure; FTIR spectrum; imidazole; intermolecular interactions; multicomponent reaction; thermo gram

Introduction

Multicomponent reactions (MCRs) have attracted great interest in modern organic synthesis and medicinal chemistry in recent years because they are one-pot processes bringing together three or more components and show high atom economy and high selectivity.

Imidazole ring has been of great interest for the organic chemist due to their useful biological and pharmacological aspects. The imidazole ring system is one of the most important substructures and incorporated in a multitude of natural products and pharmacologically active compounds such as the hypnotic agent etomidate [1], and the proton pump inhibitor omeprazole [2]. From the literature, substituted imidazoles are known as inhibitors of fungicides and herbicides, plant growth regulators, therapeutic agents, anticancer, and anti-viral agents [3]. Some imidazole derivatives are found to be having a diverse activity like anti-inflammatory, cardiovascular activity [4,5], antimicrobial activity [6], anti-fungal activity [7], and anti-viral activity. Recently, tetrasubstituted imidazole scaffold has been a core element in many biological systems like potent and specific ATP-mimetic inhibitors of p38 MAP Kinase, as p38α mitogen-activated protein kinase inhibitors [8].

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Table 1. Elemental analysis for $C_{30}H_{25}FN_2O_3$

Element	Experimental (%)	Calculated (%)
Carbon	74.99	74.98
Nitrogen	5.80	5.83
Hydrogen	5.21	5.24

Due to the importance of imidazole, many synthesis strategies have been developed. 2,4,5-triphenyl imidazoles was synthesized by 1, 2-dicarbonyl compound, various aldehydes, and ammonia in 1882 [9]. Crystal structure of the similar 2,4,5-triphenyl [10,11] and 1,2,4,5-tetraphenyl imidazole [12,13] was reported in the literature. The title compound was synthesized via four-component single-pot condensation of a benzil with a substituted benzaldehyde, ammonium acetate, and aniline.

As a result, encouraged by these pharmacological properties of imidazole and in continuation of our interest in the synthesis of biologically active imidazole analogs, we have synthesized the title compound and report the spectroscopic, crystal structure using single-crystal X-ray diffraction.

Experimental

Materials and Methods

All chemicals were purchased commercially and used without prior purification. Infrared spectra were recorded on a FT-IR spectrophotometer (SHIMADZU FT-IR spectrometer Prestige-21) in the range 400–4000 cm^{-1} using the KBr pellets. A TA-SQT Q600 thermogravimetric analyzer was used to obtain TGA curve under nitrogen atmosphere with a

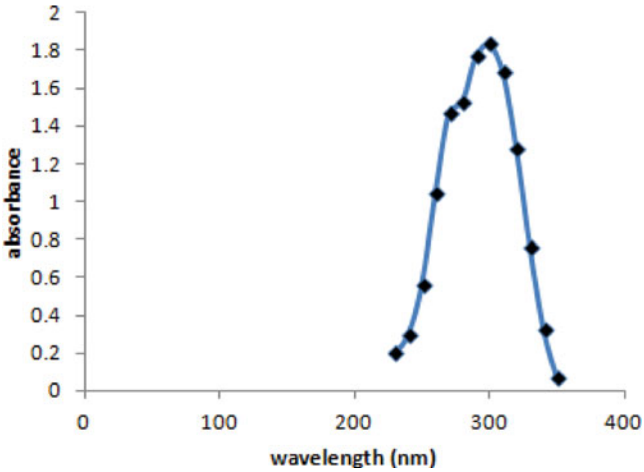


Figure 1. UV-visible spectrum of the crystal.

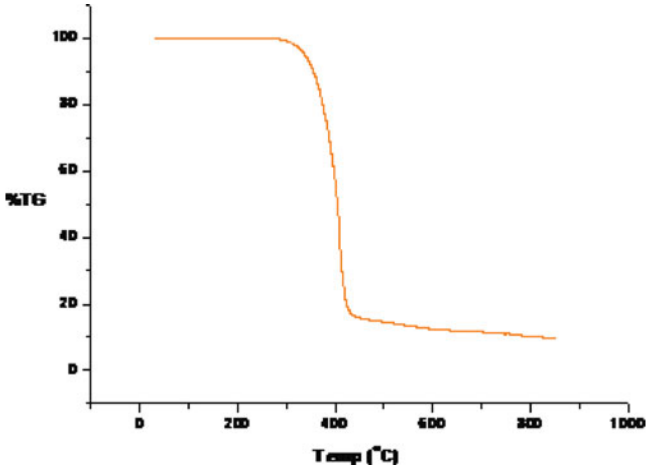


Figure 2. TGA curve of crystal.

heating rate of 20°C min^{-1}. The UV-Vis spectrum was recorded in UV-Visible spectrophotometer (SHIMADZU, UV 2550, Japan). Elemental analysis was carried out by using VARIO EL-III (Elementar Analysensysteme GmBH).

Synthesis of Compound 2-(3,4,5-trimethoxyphenyl)-1-(4-fluorophenyl)-4,5-diphenyl-1H-imidazole

Benzil (10 mmol), 3,4,5-trimethoxy benzaldehyde (10 mmol), 4-fluoroaniline (10 mmol), and ammonium acetate (12 mmol) were dissolved in boiling glacial acetic acid and refluxed for 6-8 hr. The reaction progress was monitored by thin layer chromatography (TLC). After the completion of the reaction, the reaction mixture was poured into ice water, the obtained compound was recrystallized from dimethylformamide. The synthetic strategy of the title compound is depicted in Scheme 1.

Product as white crystals (3.97 g, 83%) [m.p. 182°C–185°C].

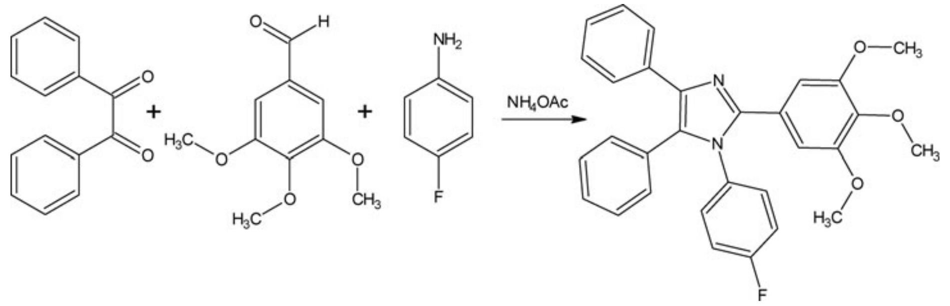
Results and Discussion

Elemental Analysis

In order to confirm the chemical composition of the synthesized compound, carbon (C), hydrogen (H), and nitrogen (N) analysis was carried out. 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 were very close to each other and within the experimental errors. This confirms the formation of the product in the stoichiometric proportion.

UV-Vis Spectral Analysis

The UV-Vis spectrum of the compound was shown in Fig. 1. The UV-Vis spectrum was recorded by using dimethylformamide as a solvent. From the graph, it was observed that



Scheme 1. 2-(3,4,5-trimethoxyphenyl)-1-(4-fluorophenyl)-4,5-diphenyl-1*H*-imidazole.

the compound shows an absorption peak at 298 nm. The transmittance of the compound is due to then-π^* transition of the constituent –OCH$_3$ group. scheme 1

Thermal Gravimetric Analysis (TGA)

The compound decomposes mainly in one stage on heating between 350°C and 420°C as shown in Fig. 2. There was no much weight loss observed around 140°C, which shows the absence of moisture in the crystal. A weight loss of around 9% occurs within 350°C indicative of the loss of one molecule of –OCH$_3$ from a compound and the maximum about 75% weight loss between the 350°C and 420°C account for the removal of four phenyl rings. Above 450°C, 15% of the residue was left out, which was due to the charring

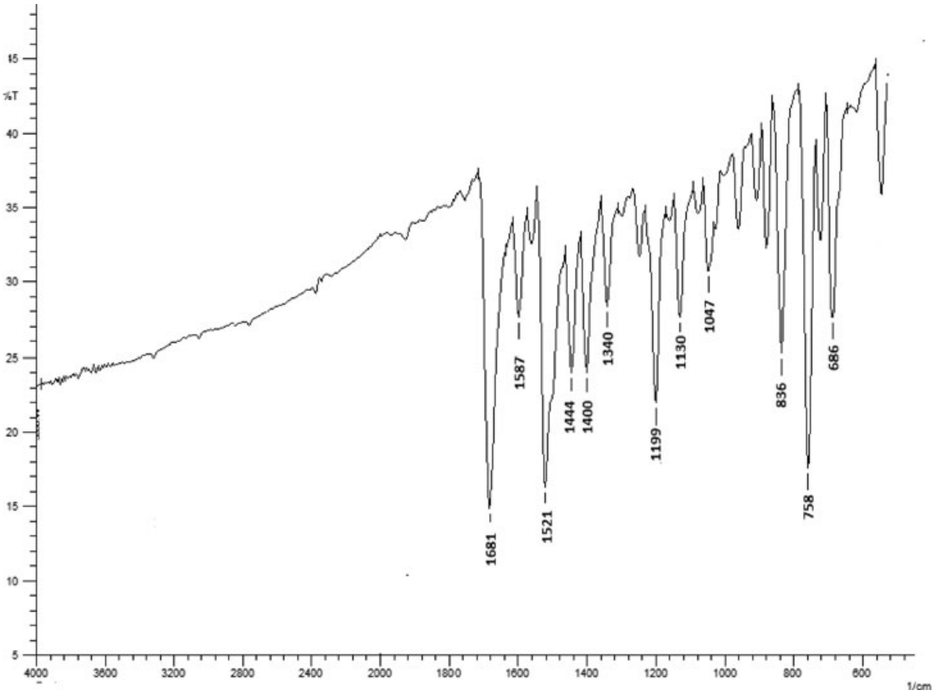


Figure 3. FTIR spectrum of the crystal.

Table 2. Crystal data and structure refinement

CCDC deposition number	931149
Empirical formula	$C_{30}H_{25}FN_2O_3$
Formula weight	480.52
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, $P\bar{1}$
Unit cell dimensions	$a = 10.286(2)$ Å $\alpha = 100.270(3)°$
	$b = 11.795(2)$ Å $\beta = 90.093(3)°$
	$c = 21.331(4)$ Å $\gamma = 90.062(3)°$
Volume	2546.5(9) $Å^3$
Z, Calculated density	4, 1.253 Mg m^{-3}
Absorption coefficient	0.086 mm^{-1}
$F_{(000)}$	1008
Crystal size	0.20 × 0.20 × 0.18 mm
Theta range for data collection	1.75°–25.35°
Limiting indices	$-12 \le h \le 12, -14 \le k \le 14, -25 \le l \le 25$
Reflections collected/unique	24531/9279 [R(int) = 0.0280]
Completeness to theta = 25.35	99.9%
Refinement method	Full-matrix least square on F^2
Data/restraints/parameters	9279/0/655
Goodness of fit on F^2	1.029
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0479$, $wR_2 = 0.1116$
R indices (all data)	$R_1 = 0.0672$, $wR_2 = 0.1221$
Largest diff. peak and hole	0.150 and −0.189 e.$Å^{-3}$

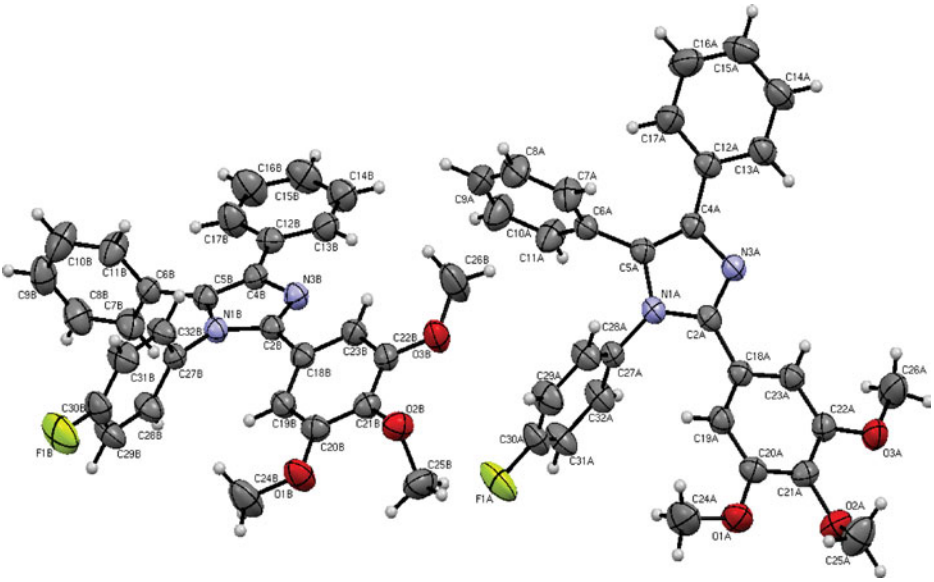


Figure 4. *ORTEP* diagram of the title molecule with 50% probability displacement thermal ellipsoids.

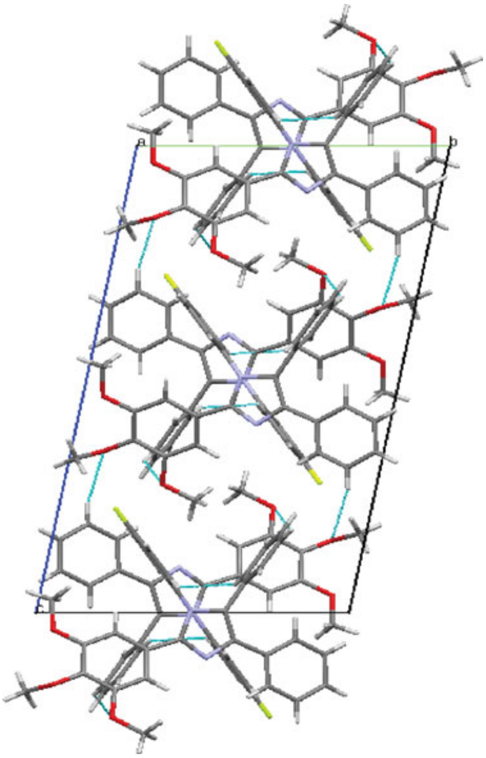


Figure 5. Packing of molecules when viewed down the *a*-axis. Dashed lines indicate hydrogen-bond interactions.

of carbon or due the imidazole ring. Thus, the TG study confirms the formation of the compound in the stoichiometric ratio.

FT-IR Spectral Analysis

The Fourier transform infrared spectroscopy (FT-IR) spectrum of the crystal structure was shown in Fig. 3. The peak at 1681 cm^{-1} was corresponded to the C=N asymmetric stretching vibration. The peaks observed at 1340 cm^{-1} were assigned for the C−N stretching,

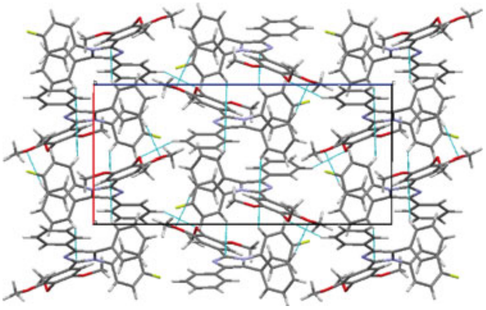


Figure 6. Packing of molecules when viewed down the *b*-axis. Dashed lines indicate hydrogen-bond interactions.

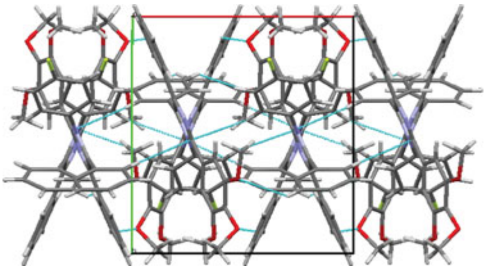


Figure 7. Packing of molecules when viewed down the *c*-axis. Dashed lines indicate hydrogen-bond interactions.

1130 cm^{-1} for the C—O stretching vibration, and 1047 cm^{-1} were assigned for the C—F stretching.

Single-Crystal X-Ray Diffraction Method

Single crystal of the suitable size of the title compound was selected for data collection. X-ray intensity data were collected on Oxford Xcalibur Eos (Nova) CCD diffractometer with X-ray generator operating at 50 kV and 1 mA, using MoK$_\alpha$ radiation (λ=0.7107 Å) [14]. Data were collected for 606 frames per set with different settings of ϕ (0°, 90°, 180°), keeping the sample to detector distance of 60.62 mm and the 2θ value fixed at 25°. A complete dataset is reduced using the software CrysAlis PRO [15]. The structure was solved by direct methods and refined by full-matrix least-square method on F^2 using SHELXS and SHELXL programs [16]. All hydrogen atoms were positioned geometrically and refined using a riding model. The geometrical calculations were carried out using the program PLATON [17]. The molecular and packing diagrams were generated using the software MERCURY [18].

The crystal data and structure refinement details are reported in Table 2.

The Oak Ridge Thermal Ellipsoid Plot (*ORTEP*) diagram of the molecule with 50% probability displacement thermal ellipsoids is shown in Fig. 4.

The packing of molecules when viewed down *a*-axis, *b*-axis, and *c*-axis is given in Figs. 5, 6, and 7, respectively.

Two symmetry-independent molecules (**A** and **B**) are present in the asymmetric unit, consisting of an imidazole ring, two phenyl rings, a methoxy-substituted phenyl ring, and a fluorine-substituted phenyl ring.

The methoxy-substituted phenyl ring forms a dihedral angle of 22.09(9)° in molecule **A** and 22.20(9)° in molecule **B** with respect to imidazole ring, corresponding to axial position. However, phenyl ring C6A/C7A/C8A/C9A/C10A/C11A of molecule **A** and phenyl ring C6B/C7B/C8B/C9B/C10B/C11B of molecule **B** are in equatorial positions with respect to imidazole ring N1A/C2A/N3A/C4A/C5A of molecule **A** and N1B/C2B/N3B/C4B/C5B of molecule **B**, as confirmed by the similar dihedral angles 79.40(10)°, which deviates from the dihedral angle value of 68.2(3)° reported earlier for the similar molecular structure of 1-(4-chlorophenyl)-4,5-diphenyl-2-(3,4,5-trimethoxyphenyl)-1H-imidazole [12].

A dihedral angle of 2.60(10)° is observed between phenyl ring C12A/C13A/C14A/C15A/C16A/C17A and the imidazole ring N1A/C2A/N3A/C4A/C5A of molecule **A** and between phenyl ring C12B/C13B/C14B/C15B/C16B/C17B and imidazole ring

Table 3. Selected bond lengths and bond angles [Å, °]

F1A—C14A	1.360(2)	O3B—C4B	1.365(2)
F1B—C14B	1.360(2)	O3B—C10B	1.415(3)
O1A—C6A	1.373(2)	N1A—C11A	1.442(2)
O1A—C8A	1.425(3)	N1A—C1A	1.375(2)
O2A—C9A	1.432(3)	N1A—C24A	1.393(2)
O2A—C5A	1.373(2)	N2A—C17A	1.380(2)
O3A—C10A	1.417(3)	N2A—C1A	1.318(2)
O3A—C4A	1.361(2)	N1B—C24B	1.394(2)
O1B—C8B	1.424(3)	N1B—C11B	1.438(2)
O1B—C6B	1.367(2)	N1B—C1B	1.378(2)
O2B—C5B	1.373(2)	N2B—C1B	1.320(2)
O2B—C9B	1.428(3)	N2B—C17B	1.380(2)
C6A—O1A—C8A	117.09(16)	N1A—C11A—C16A	119.53(15)
C5A—O2A—C9A	114.80(15)	F1A—C14A—C15A	118.45(18)
C4A—O3A—C10A	118.57(16)	F1A—C14A—C13A	118.44(18)
C6B—O1B—C8B	116.79(16)	N2A—C17A—C24A	110.10(15)
C5B—O2B—C9B	114.87(15)	N2A—C17A—C18A	119.05(15)
C4B—O3B—C10B	118.45(16)	N1A—C24A—C17A	105.38(14)
C1A—N1A—C11A	128.11(14)	N1A—C24A—C25A	121.51(15)
C1A—N1A—C24A	107.18(13)	N1B—C1B—N2B	110.87(15)
C11A—N1A—C24A	124.63(14)	N1B—C1B—C2B	126.56(15)
C1A—N2A—C17A	106.59(14)	N2B—C1B—C2B	122.57(15)
C1B—N1B—C11B	128.19(14)	O3B—C4B—C3B	123.92(17)
C1B—N1B—C24B	106.86(13)	O3B—C4B—C5B	115.52(16)
C11B—N1B—C24B	124.86(13)	O2B—C5B—C4B	121.39(16)
C1B—N2B—C17B	106.68(14)	O2B—C5B—C6B	119.20(16)
N1A—C1A—N2A	110.75(15)	O1B—C6B—C5B	115.69(16)
N1A—C1A—C2A	126.76(15)	O1B—C6B—C7B	124.14(17)
N2A—C1A—C2A	122.49(15)	N1B—C11B—C12B	119.82(15)
O3A—C4A—C3A	123.87(17)	N1B—C11B—C16B	119.98(15)
O3A—C4A—C5A	115.82(16)	F1B—C14B—C13B	118.45(18)
O2A—C5A—C6A	119.21(16)	F1B—C14B—C15B	118.60(18)
O2A—C5A—C4A	121.27(16)	N2B—C17B—C18B	119.11(15)
O1A—C6A—C5A	115.88(16)	N2B—C17B—C24B	109.89(15)
O1A—C6A—C7A	123.87(16)	N1B—C24B—C17B	105.70(14)
N1A—C11A—C12A	120.19(15)	N1B—C24B—C25B	121.33(15)

N1B/C2B/N3B/C4B/C5B of molecule **B**, which shows that they have occupied the axial positions. These values of dihedral angles deviate much from 41.7(1)°, reported earlier for the molecular structure 2-(2-methylphenyl)-4,5-diphenyl-1H-imidazole [19]. A dihedral angle of 45.01(10)° between imidazole rings in molecule **A** and in molecule **B** shows that they are in bisectional positions. The fluorine-substituted phenyl ring forms a dihedral angle of 72.59(10)° in molecule **A** and molecule **B** with respect to imidazole ring, corresponding to equatorial position. Overall, two molecules **A** and **B** in the asymmetric unit are geometrically identical with one another.

Table 4. Selected torsion angles [°]

N(3A)–C(2A)–C(18A)–C(23A)	−21.4(2)
N(1A)–C(2A)–C(18A)–C(23A)	158.72(16)
N(3A)–C(2A)–C(18A)–C(19A)	156.56(17)
N(1A)–C(2A)–C(18A)–C(19A)	−23.4(3)
C(2A)–N(1A)–C(27A)–C(28A)	108.9(2)
C(5A)–N(1A)–C(27A)–C(28A)	−74.7(2)
C(2A)–N(1A)–C(27A)–C(32A)	−70.5(2)
C(5A)–N(1A)–C(27A)–C(32A)	105.9(2)
C(23B)–C(18B)–C(2B)–N(3B)	21.5(2)
C(19B)–C(18B)–C(2B)–N(3B)	−156.31(17)
C(23B)–C(18B)–C(2B)–N(1B)	−158.78(16)
C(19B)–C(18B)–C(2B)–N(1B)	23.4(3)
C(4B)–C(5B)–C(6B)–C(11B)	−99.1(2)
N(1B)–C(5B)–C(6B)–C(11B)	79.7(2)
C(4B)–C(5B)–C(6B)–C(7B)	79.0(3)
N(1B)–C(5B)–C(6B)–C(7B)	−102.3(2)
C(25A)–O(2A)–C(21A)–C(22A)	113.0(2)
C(25A)–O(2A)–C(21A)–C(20A)	−71.4(2)
C(2B)–N(1B)–C(27B)–C(32B)	70.5(2)
C(5B)–N(1B)–C(27B)–C(32B)	−105.6(2)
C(2B)–N(1B)–C(27B)–C(28B)	−108.9(2)
C(5B)–N(1B)–C(27B)–C(28B)	75.0(2)
C(4A)–C(5A)–C(6A)–C(11A)	98.8(2)
N(1A)–C(5A)–C(6A)–C(11A)	−79.7(2)
C(4A)–C(5A)–C(6A)–C(7A)	−79.5(3)
N(1A)–C(5A)–C(6A)–C(7A)	102.0(2)
C(25B)–O(2B)–C(21B)–C(20B)	71.6(2)
C(25B)–O(2B)–C(21B)–C(22B)	−113.0(2)

Bond lengths, bond angles, and torsion angles are given in Tables 3 and 4. Hydrogen-bond geometry is listed in Table 5.

The molecular structure involves C_g–C_g interactions between the ring N1A/C2A/N3A/C4A/C5A and its adjacent ring N1A/C2A/N3A/C4A/C5A in the asymmetric unit with a centroid–centroid distance of 5.943(15) Å, slippage of 3.521 Å, and symmetry code, $1-x$, $1-y$, $-z$. The crystal structure is stabilized by the interactions: C25A–H25C···C_g3 (where

Table 5. Hydrogen-bond geometry [Å, °]

D–H···A	d(D–H)	d(H···A)	d(D···A)	<(DHA)
C(13A)–H(13A)···N(3A)[a]	0.93	2.46	2.819(2)	103
C(13B)–H(13B)···N(3B)[a]	0.93	2.46	2.818(2)	103
C(23A)–H(23A)···N(3A)[a]	0.93	2.53	2.842(2)	100
C(23B)–H(23B)···N(3B)[a]	0.93	2.53	2.847(2)	100
C(25A)–H(25C)···O(1A)[a]	0.96	2.40	2.977(3)	118
C(25B)–H(25D)···O(1B)[a]	0.96	2.39	2.973(3)	118

[a] Intra-molecular hydrogen-bond interaction.

C_g3 is C12A/C13A/C14A/C15A/C16A/C17A with a symmetry code x, $1+y$, z) with a C–C_g distance of 3.551(2) Å, C–H···C_g angle of 127°, and C25B–H25D···C_g8 (where C_g8 is C12B/C13B/C14B/C15B/C16B/C17B with a symmetry code x, $1+y$, z) with a C–C_g distance of 3.548(2) Å, C–H···C_g angle of 127°.

The molecular structure of the title molecule is stabilized by the intra-molecular interactions of types C—H···N and C—H···O.

Conclusion

Single crystal was grown by the slow evaporation method. The elemental analysis confirms the formation of the compound in a stoichiometric ratio. The UV-Vis spectrum reveals the properties of the crystals. TGA was carried out to study the thermal behavior of the crystal. The FTIR spectrum characterizes the presence of various functional groups. The single-crystal X-ray diffraction study indicates that the compound crystallizes in the triclinic crystal system.

Acknowledgment

The authors gratefully acknowledge the UGC and DST-PURSE for the financial assistance and Mangalore University, USIC for their instrumental facilities.

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