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Crystal Structure of (*E*)-1-(4-fluorobenzylidene)-2-(2,3-dihydro-1-isobutyl-1H-naphtho[2,1-d]imidazol-4-yl)hydrazine

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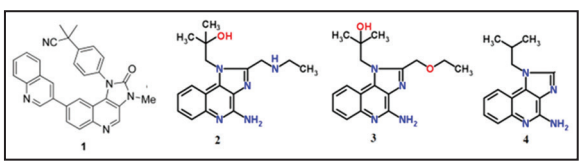
ABSTRACT

The title compound, 1-(4-fluorobenzylidene)-2-(2,3-dihydro-1-isobutyl-1H-naphtho[2,1-d]imidazol-4-yl) hydrazine ($C_{21}H_{24}FN_5O$) was synthesized and characterized by spectroscopic techniques and finally the structure was confirmed by X-ray diffraction studies. The title compound crystallized in the monoclinic crystal system, in the space group $P2_1/n$. The unit cell parameters are a=10.4209 (16) Å, b=18.179 (4) Å, c=11.945 (2) Å, β=114.674 (1)°, Z=4 and V=2056.3 (7) Å^3. The structure adopts an E conformation with respect to the C=N bond. The compound exhibits intermolecular interaction of the type O-H…N with symmetry code ½+x, ½−y, −½+z, N-H…O with symmetry code −½+x, ½−y, ½+z, and C-H…O with symmetry code ½+x, ½−y, ½+z.

Key words: *Crystal structure, Schiff base, Monoclinic crystal.*

1. INTRODUCTION

Fused heterocycles are bestowed with properties due to their respective structural units. They also acquire additional attributes owing to changed electronic environment. Most frequently encountered examples in the area of fused heterocycles are indole, quinoline, imidazole, and isoquinoline [1]. Compound NVP-BEZ235 (1) as a starting point for antitrypanosomal drug discovery and a potent inhibitor of human phospoinositide-3-kinases and mammalian target of rapamycin [2]. The core structure is 1H-imidazo[4,5-c] quinoline like in gardiquimod (2), resiquimod (3), and imiquimod (4), which acts as an immune response modifier and also shows antiviral, anti-tumor and anti-inflammatory activities [3-5]. The 1*H*-imidazo[4,5-c] quinolines are an important class of N-tricyclic compounds. These compounds are also known as Imidazolquinoline. The synthesis of imidazoquinoline had been of increasing interest since many of their derivatives exhibited useful applications such as antimalarial [6], anticonvulsant and antitumor agents [7].



Schiff bases are important for medicines in aspect of theoretical and practical views [8,9]. Schiff bases have remarkable complex-forming properties and serve as excellent chelating ligands and have been used as analytical reagents for the spectrophotometric determination of metal ions [10]. Attributed to the above fact and with a view to obtain new and better biological active agent, we thought to synthesized (*E*)-1-(4-fluorobenzylidene)-2-(2,3-dihydro-1-isobutyl-1*H*-naphtho[2,1-d]imidazol-4-yl)hydrazine by condensation of 4-hydrazino-1-isobutyl-1H-imidazole[4,5c] quinoline and 4-fluoro benzaldehyde. Furthermore, to characterize the novel compound with X-ray diffraction studies.

2. EXPERIMENTAL

2.1. Materials and Methods

All solvents and reagents were purchased from Sigma-Aldrich Chemicals Pvt. Ltd. and Merck. Melting range was determined by Veego Melting Point VMP III apparatus.

2.2. Synthesis of (E)-1-(4-fluorobenzylidene)-2-(2,3-dihydro-1-isobutyl-1H-naphtho[2,1-d]imidazol-4-yl) hydrazine (3)

Equimolar concentrations of 4-hydrazino-1-iso butyl-1*H*-imidazo[4,5-c]quinoline (1) (0.01 mol), and the 2-fluoro benzaldehyde (2) (0.01 mol) were refluxed

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for 7-8 h using methanol (20 ml), and 2-3 drops of glacial acetic acid were added to the mixture. The progress of the reaction was followed by thin layer chromatography until the reaction was complete. It was cooled to 0°C; the precipitate was filtered, dried, and recrystallized from ethanol. Mp: 218-215°C.

2.3. X-ray Crystallography

A crystal of suitable dimensions was selected for X-ray structure analysis. The diffraction intensity data were collected on a Bruker CCD diffractometer equipped with Cu Kα radiation. Data reduction and applying of absorption corrections were carried out using the APEX 2 package [11]. Crystal structure was solved by direct methods using SHELXS-97 and was refined by full matrix least squares refinement against F^2 using SHELXL-97 [12]. All the non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were placed at chemically acceptable positions.

3. RESULT AND DISCUSSION

Synthesis of 1-(4-fluorobenzylidene)-2-(2,3-dihydro-1-isobutyl-1H-naphtho[2,1-d]imidazol-4-yl)hydrazine from the condensation reaction of 4-hydrazino-1-isobutyl-1*H*-imidazo[4,5-c]quinoline and the 2-fluoro benzaldehyde. The molecular structure of compound (3) is given in Figure 1 with numbering scheme.

The structures of the title compound have been confirmed by single crystal X-ray diffraction analysis. The bond lengths and bond angles are in good agreement with the standard values, and the list of selected bond lengths and bond angles are given in Tables 1 and 2, respectively. The oak ridge thermal ellipsoid plot diagram of the compound is shown in Figure 1. Intermolecular and intramolecular hydrogen bonding distances for compounds and their torsion angles are listed in Tables 3 and 4, respectively.

Title compound crystallizes in monoclinic crystal system ($\alpha = \gamma = 90$, $\beta \neq 90$) with the space group $P2_1/n$; the crystal packing in unit cell is stabilized by intermolecular O-H…N with symmetry code ½+*x*, ½−*y*, −½+*z*, N-H…O with symmetry code −½+*x*, ½−*y*, ½+*z* and C-H…O with symmetry code ½+*x*, ½−*y*, ½+*z*. A total of 260 parameters were refined with 2698 unique reflections which converged the residual to R=0.0700. The bond lengths and bond angles values are within the expected range. The unit cell parameters

Table 1: Selected bond lengths (Å) of title compound.

Atoms	Length	Atoms	Length
F1-C19	1.3728	C6-C10	1.4210
N1-C5	1.3550	C7-C8	1.4237
N1-C4	1.4677	C8-C9	1.4052
N1-C7	1.3886	C8-C11	1.4059
N2-C6	1.3837	C9-C14	1.4106
N2-C5	1.2994	C11-C12	1.3620
N3-C10	1.3055	C12-C13	1.3851
N3-C9	1.3866	C13-C14	1.3663
N4-C10	1.3743	C15-C16	1.4413
N4-N5	1.3628	C16-C21	1.3923
N5-C15	1.2529	C16-C17	1.3912
C2-C3	1.4977	C18-C19	1.3415
C2-C4	1.5125	C19-C20	1.3611
C6-C7	1.3646	C20-C21	1.3995

Table 2: Selected bond angles (°).

Atoms	Angle	Atoms	Angle
C4-N1-C7	128.68	N3-C9-C8	124.28
C5-N1-C7	106.18	N3-C9-C14	117.11
C4-N1-C5	124.85	C8-C9-C14	118.60
C5-N2-C6	104.55	N3-C10-N4	121.11
C9-N3-C10	119.86	N4-C10-C6	119.18
N5-N4-C10	119.49	N3-C10-C6	119.70
N4-N5-C15	117.96	C8-C11-C12	121.36
C1-C2-C3	112.34	C11-C12-C13	119.41
C1-C2-C4	109.27	C12-C13-C14	121.23
C3-C2-C4	111.55	C9-C14-C13	120.29
N1-C4-C2	112.63	N5-C15-C16	122.59
N1-C5-N2	113.36	C15-C16-C21	120.85
N2-C6-C10	128.09	C17-C16-C21	118.14
C7-C6-C10	121.16	C15-C16-C17	120.9
C7-C6-C10	121.16	C16-C17-C18	120.86
N2-C6-C7	110.75	C17-C18-C19	119.15
N1-C7-C8	134.07	F1-C19-C18	118.7
C6-C7-C8	120.77	F1-C19-C20	117.91
N1-C7-C6	105.15	C18-C19-C20	123.32
C7-C8-C11	126.85	C19-C20-C21	117.87
C9-C8-C11	118.93	C16-C21-C20	120.62

Table 3: Hydrogen-bond geometry (Å, °).

Symmetry code				
D—H...A	D—H	H...A	D...A	D—H...A
O(1)-H(1B)...N(3)	0.85	2.40	2.9723	125
½+*x*, ½−*y*, −½+*z*				
N(2-) H(3AA)...O(1)	0.86	2.36	2.9567	127
½−*x*, ½+*y*, ½−*z*				
C(5)-H(5AA)...O(1)	0.93	2.46	3.3052	151
½+*x*, ½−*y*, ½+*z*				

are a=10.4209 (16) Å, b=18.179 (4) Å, c=11.945 (2) Å, β=114.674 (1)°, Z=4 and V=2056.3 (7) Å^3. The data pertinent to crystal structure determination are summarized in Table 5.

Figure 2a and b show the packing diagrams viewed down a and b axes, respectively. The geometrical calculations were carried out using the program Platon [13]. The molecular and packing diagrams were generated using Mercury [14]. The compound contains one benzene ring, and fused heterocycle is bridged by a C=N imino moiety. The molecule exists in the solid state in an E-configuration with respect to the C15=N5 bond as indicated by the torsion angle C16-C15-N5-N4=178.47. The conformation of the attachments of the fused heterocyclic ring and the straight C-chain group are well defined by the torsion angle values of 61.38°C3-C2-C4-N1, which is evident that they adopt gauche staggered conformation.

4. CONCLUSION

In view of the importance of fused heterocyclic units which possess diverse biological and physical properties, the title compound was synthesized. X-ray diffraction study reveals that the title compound crystallized in the monoclinic crystal system, in the space group P2$_1$/n. The structure adopts an E conformation with respect to the C=N bond. The crystal structure studies show the existence of intermolecular O-H…N, N-H…O, and C-H…O types H-bonding.

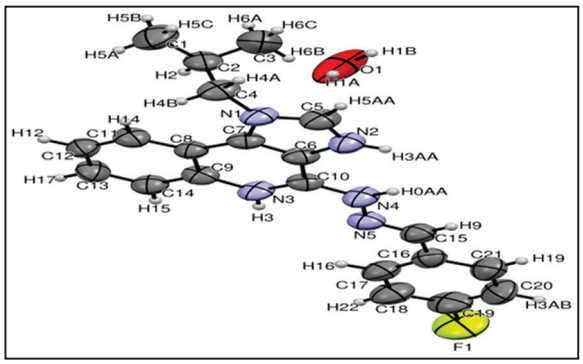

Figure 1: The oak ridge thermal ellipsoid plot diagram of the title compound with labeling scheme.

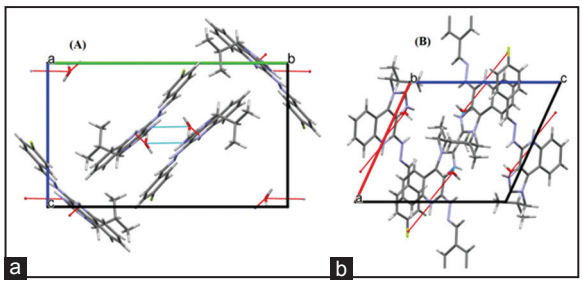

Figure 2: The molecular packing view of the title compound down the a and b axis respectively.

Table 4: Selected torsion angles (°).

Atoms	Angle	Atoms	Angle
C5-N1-C7-C8	179.20	N2-C6-C10-N4	−0.20
C7-N1-C4-C2	69.19	N1-C7-C8-C9	−176.75
C4-N1-C5-N2	174.52	C6-C7-C8-C9	1.65
C5-N1-C4-C2	−103.86	N1-C7-C8-C11	5.14
C4-N1-C7-C8	5.14	C6-C7-C8-C11	−176.46
C4-N1-C7-C6	−173.44	C7-C8-C9-C14	176.60
C7-N1-C5-N2	0.17	C7-C8-C11-C12	−178.51
C5-N1-C7-C6	0.63	C9-C8-C11-C12	3.46
C5-N2-C6-C7	1.28	C7-C8-C9-N3	−2.02
C5-N2-C6-C10	−178.58	C11-C8-C9-N3	176.25
C6-N2-C5-N1	−0.87	C11-C8-C9-C14	−5.13
C10-N3-C9-C8	0.74	C8-C9-C14-C13	3.38
C10-N3-C9-C14	−177.90	C8-C11-C12-C13	0.13
C9-N3-C10-N4	179.72	N3-C9-C14-C13	−177.91
C9-N3-C10-C6	0.98	C11-C12-C13-C14	−2.02
C10-N4-N5-C15	−178.32	C12-C13-C14-C9	0.22
N5-N4-C10-C6	177.04	N5-C15-C16-C17	4.34
N5-N4-C10-N3	−1.71	N5-C15-C16-C21	−173.88
N4-N5-C15-C16	178.47	C15-C16-C17-C18	−177.54
C1-C2-C4-N1	−173.79	C21-C16-C17-C18	0.72
C3-C2-C4-N1	61.38	C15-C16-C21-C20	177.71
N2-C6-C7-C8	−179.98	C17-C16-C21-C20	−0.56
N2-C6-C10-N3	178.56	C16-C17-C18-C19	0.43
C10-C6-C7-C8	−0.13	C17-C18-C19-F1	178.95
N2-C6-C7-N1	−1.19	C17-C18-C19-C2	−1.84
C7-C6-C10-N4	179.95	F1-C19-C20-C21	−178.81
C10-C6-C7-N1	178.68	C18-C19-C20-C21	1.98

Table 5: Crystal data and structure refinement details.

Parameter	Value
CCDC deposit no.	1469530
Empirical formula	$C_{21}H_{24}FN_5H_2O$
Formula weight	381.45
Temperature	293 (2) K
Wavelength	1.54178 Å
Crystal system, space group	Monoclinic, P2$_1$/n
Unit cell dimensions	a=10.4209 (16)Å b=18.179 (4) Å c=11.945 (2) Å α=90° β=114.6741 (12)° γ=90°
Volume	2056.2 (7) Å^3
Z	4
Density (calculated)	1.232 mg m^{-3}

(Contd...)

Table 5: ***(Continued)***

Parameter	Value
Absorption coefficient	0.695 mm^{-1}
F 000	808
Crystal size	0.25 mm×0.25 mm× 0.25 mm
θ range for data collection	7.38-64.00°
Index ranges	−7≤h≤12 −19≤k≤21 −10≤l≤13
Reflections collected	5877
Independent reflections	2698 (R int.=0.0700)
Absorption correction	None
Refinement method	Full matrix least-squares on F^2
Data/restraints/para meters	2698/0/260
Goodness-of-fit on F^2	1.051
Final [I>2σ(I)]	R1=0.08941, wR2=0.2371
R indices (all data)	R1=0.1798, wR2=0.2998
Largest difference peak and hole	0.507 and−0.389 e $Å^{-3}$

5. ACKNOWLEDGMENTS

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***Bibliographical Sketch**

Dr. N. K. Lokanath obtained his MSc and PhD in Physics from the University of Mysore, Mysore. Presently he is working as a Professor at Department of Studies in Physics, University of Mysore, India. Recently, he was awarded the prestigious Sir C V. Raman Young Scientist's State award from Government of Karnataka for his outstanding contribution towards science. Prof. Lokanath's area of research includes structural biology, chemical biology, and structural studies of B-Z junction DNA, enzymes and new materials. He solved the first crystal structure of subunit E of A-ATPase from Pyrococcus horikoshii which was acclaimed worldwide as a significant finding. He has determined structures of more than 75 proteins and has published more than 150 articles in Journals of International repute and has delivered more than 50 lectures in India and across the world. Dr. Lokanath is a member of many professional bodies and he is also a Visiting Professor at the Sungkyunkwan University School of Medicine, South Korea.