DOI: 10.7598/cst2018.367
ISSN:2278-3458

Chemical Science Transactions
2018, **7(1),** 71-76

RESEARCH ARTICLE

Crystal and Molecular Structure of 2-(2-Fluoro-phenyl)-1*H*-benzoimidazole

MOHAMED ZIAULLA, AFSHAN BANU and NOOR SHAHINA BEGUM*

Department of Chemistry, Bangalore University, Bangalore-560001, India
noorsb@rediffmail.com

Received 31 August 2012 / Accepted 9 October 2017

Abstract: The crystal structure analysis of 2-(2-fluoro-phenyl)-1*H*-benzoimidazole is described. The benzoimidazole and fluorophenyl rings are non-coplanar with the dihedral angle $34.25(3)^0$. The crystal packing exhibits intramolecular N-H…F and intermolecular N-H…N, C-H…F, π-π stacking interactions leading to the formation of the supramolecular network.

Keywords: Benzoimidazole derivative, Crystal structure, N-H…F, N-H…N, C-H…F and π-π Weak interactions

Introduction

Benzoimidazole is important bioactive molecule in pharmaceutical fields[1]. Not only can they be used for producing medicines such as omeprazole and pimobendan, but also have they exhibited significant activities against some viruses including RSV[2], herpes (HCV)[3], HIV[4] and human cytomegalovirus (HCMV)[5]. Benzoimidazoles and their derivatives exhibit a number of important pharmacological properties, such as antihistaminic[6], anti-ulcerative[7], antiallergic[8] and antipyretic[9]. In addition, benzoimidazole derivatives are effective against the human cytomegalovirus (HCMV)[10] and are also efficient selective neuropeptide Y Y1 receptor antagonists[11]. Most of the described methods for the synthesis of benzoimidazoles make use of volatile organic solvents and involve solid-phase synthesis via *o*-nitroanilines[12-15] or the condensation of *o*-phenylenediamines with carboxylic acid derivatives[16], aldehydes[17-22] and aryl halides[23]. The single crystal x-ray diffraction technique was obtained for this compound in view of the vast amount of structural information and its ability to decipher the complexity of crystal design.

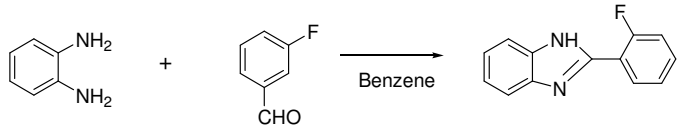
Experimental

All chemicals were obtained from a commercial source and used without further purification. Pale yellow colored single crystals suitable for x-ray diffraction were obtained by slow evaporation method using methanol as the solvent.

*Experimental procedure for the synthesis and crystallization of compound **3***

A mixture of *o*-phenylenediamine **1** (10 mmol) and *m*-fluorobenzaldehyde **2** (10 mmol) in benzene (100 mL) was refluxed for 2 h in a steam bath. On standing overnight yellow

crystalline solid precipitated (Scheme 1). The yellow solid product formed was separated by filtration and washed with a mixture of water and *n*-hexane. It was recrystallised from ethanol to get pale yellow crystals and then dried *in vacuum* over P_2O_5. The yellow product **3** is produced in 90% (2.34 mg) yield. M.p.: 115 °C.



1 **2** **3**

Scheme 1. Synthesis of 2-(2-fluoro-phenyl)-1*H*-benzoimidazole

Investigation techniques

X- ray diffraction

The x-ray diffraction data were collected on a Bruker Smart CCD area detector system[24], using MoKα (0.71073Å) radiation at 100(2) K for the crystal. Intensity data were collected up to a max of 25.99° for the compound in the ω–ϕ scan mode. The data were reduced using SAINTPLUS[24]. A total of 30734 reflections were collected, resulting in 2012 independent reflections of which the number of reflections satisfying $I>2\ \sigma(I)$ criteria were 1837. These were treated as observed. It was confirmed that the crystal belongs to monoclinic crystal system and the space group is *Pbca*. The structure was solved by direct methods and difference Fourier synthesis using SHELXS97[25]. The positions of all non-hydrogen atoms were included in the full-matrix least-square refinement using SHELXL97[25]. Anisotropic refinement using full-matrix least-square procedures was carried out for a few cycles until convergence was reached. All hydrogen atoms were located from Fourier difference maps and were refined isotropically. The C-H bond lengths are in the range of 0.95(2)-1.007(3) Å. The R factor after final convergence was 0.0373 and the maximum and minimum values of residual electron density were 0.323 and -0.181 $eÅ^{-3}$. Molecular diagrams were generated using ORTEP[26] and the packing diagrams were generated using CAMERON[27]. The mean plane calculation was done using the program PARST[28].

Results and Discussion

Summary of crystallographic data and other structure refinement parameters of the title compound are given in Table 1-2 gives the respective hydrogen bonding parameters. The ORTEP view of the molecule with atomic labeling (thermal ellipsoids drawn at 50% probability) is shown in Figure 1-3, show the packing of molecules in the crystal structure.

The benzoimidazole ring system is planar with r.m.s. deviation 0.0082Å and torsional angle of C7–N1–C1–C2 being 178.30°. The benzoimidazole and fluorophenyl rings are non-coplanar with the dihedral angle $34.25(3)^0$ (Figure 1). The bond lengths and angles for the benzoimidazole moiety of the molecule are in good agreement, within experimental errors, with those observed in other benzoimidazole derivatives[29-34]. The N2- C7 and N1-C7 distances were found to be 1.366(2)Å and 1.322(2)Å, respectively[35.] The corresponding values in 2-(3-methoxy-2-hydroxy phenyl) benzoimidazole[33] are 1.371(4)Å and 1.325(5)Å; in l-(phenylmethyl)-2-(4-methoxyphenylmethyl)-1H-benzoimidazole-5-carboxylic acid they are 1.365(4)Å and 1.331(4)Å. The molecular structure is primarily stabilized by intramolecular N-H…F hydrogen bond leading to the formation of a pseudo-six-membered hydrogen bonded pattern with graph set S(6), thus locking the molecular conformation and eliminating conformational flexibility.

Table 1. Crystal data and structure refinement of compound **3**

Empirical formula	$C_{13}H_9FN_2$
Formula weight	212.22
Temperature	100(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, *Pbca*
Unit cell dimensions	
	a = 7.0799(3) Å
	b = 9.9745(4) Å
	c = 12.9054 (3) Å
	β = 29.1080(12) °
Volume	2055.56(15) $Å^3$
Z,	8
Calculated density, Mg/m^3	1.372
Absorption coefficient, mm^{-1}	0.096
F(000)	880
Crystal size	0.30x0.22x0.20 mm
Theta range for data collection	1.40 to 25.99 deg.
Limiting indices	-8<=h<=8, -11<=k<=12, -35<=l<=35
Reflections collected / unique	30734 / 2012 [R(int) = 0.0329]
Completeness to theta	99.9%
Max. and min. transmission	0.9811 and 0.9719
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2012/0/181
Goodness-of-fit on F^2	1.006
Final R indices [I> 2sigma (I)]	R1 = 0.0373, wR2 = 0.1072
R indices (all data)	R1 = 0.0410, wR2 = 0.1101
Largest diff. peak and hole ($e.A^{-3}$)	0.323 and -0.181

Table 2. Non-bonded interactions and possible hydrogen bonds (Å,°) for compound 3. (D-donor; A-acceptor; H-hydrogen)

D-H...A	D-H	H...A	D...A	D-H...A
N2-H2N…F1[i]	0.926(2)	2.441(2)	2.784(1)	102
N2-H2N…N1 [ii]	0.926(2)	1.947(3)	2.842(2)	162
C10-H10…F1 [iii]	0.950(2)	2.413(2)	3.208(2)	141

Symmetry code: (i) x,y,z (ii) x+1/2, -y+1/2, -z (iii) -x, y+1/2, -z+1/2

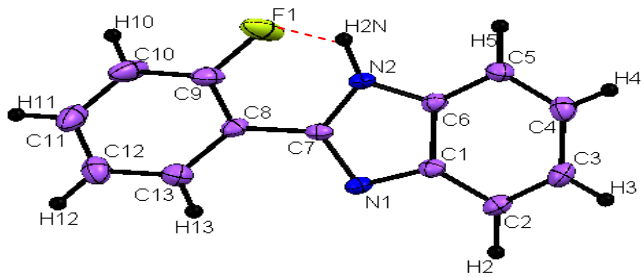


Figure 1. ORTEP view of compound **3**, showing 50% Probability ellipsoids and the atom-numbering scheme. (Dotted line indicates intramolecular N-H…F interaction)

Intermolecular features

The packing of molecules is essentially via the involvement of weak intermolecular contacts. The three dimensional framework structure by the combination of N-H…N and C-H…F intermolecular interactions stabilizes the crystal structure. The N-H…N interactions results in chain of molecules along *'a'* axis (Figure 2). The intermolecular interaction of type C-H…F creates self assembly in terms of two dimensional zig-zag tapes like pattern along crystallographic *'a'* axis (Figure 3). The molecular packing is further stabilized by π-π stacking interactions between the fluorophenyl rings. The C9-C11 disposed at a distance of 3.615(2) Å.

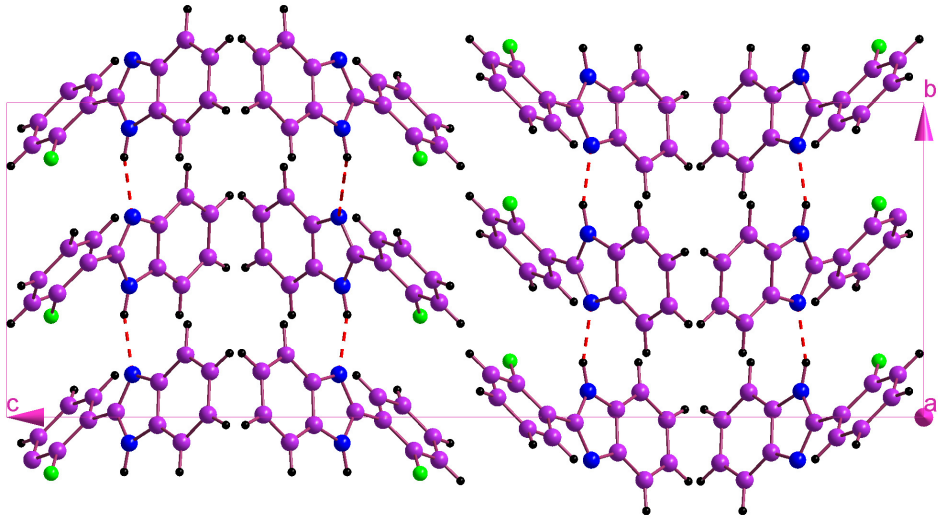


Figure 2. Hydrogen bond network in compound **3** through C-H...F bonds and N-H...N interactions

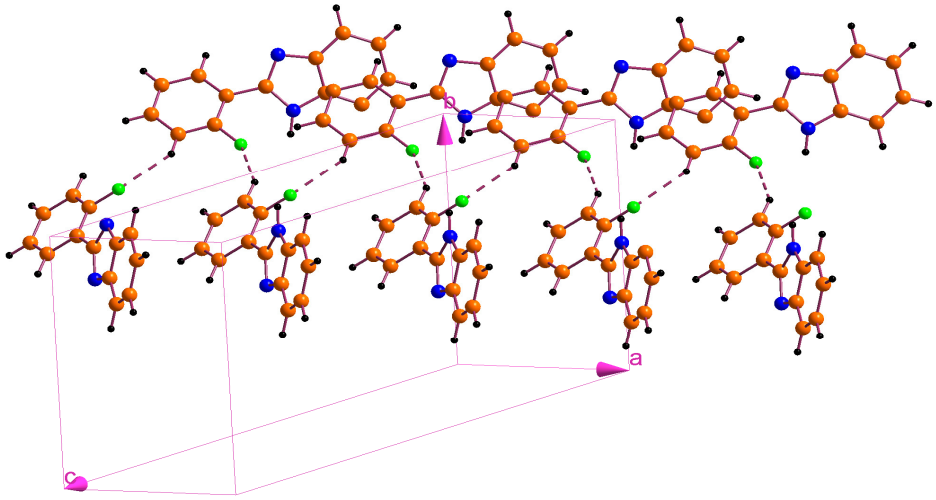


Figure 3. Packing of the molecules in crystal of **3**. Dotted lines indicate, C-H….F intermolecular interaction.

Conclusion

This work describes the synthesis of 2-(2-fluoro-phenyl)-1*H*-benzoimidazole. Additionally, the x-ray analysis was carried out in order to establish a supramolecular assembly with the specific aim of assessing various weak interactions including fluorine interaction that control the architecture of organic solids.

Acknowledgement

NSB is thankful to the University Grants Commission, Delhi for the financial assistance. They also thank the DST, for the CCD facility. Mohamed Ziaulla also thanks Impact College of Engineering and Applied Sciences, Bangalore, for their support and encouragement.

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