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Research Article

Synthesis and Crystal Structure of 6-Bromo-2-(furan-2-yl)-3-(prop-2-ynyl)-3H-imidazo[4,5-b]pyridine

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The crystal and molecular structure of 6-bromo-2-(furan-2-yl)-3-(prop-2-ynyl)-3H-imidazo[4,5-b]pyridine ($C_{13}H_8BrN_3O$) has been investigated from single crystal X-ray diffraction data. The primary focus is to investigate the molecular geometry of this compound in the solid state along with the associated intermolecular hydrogen bonding and related π-π interactions present in the crystal packing. This compound crystallizes in the monoclinic space group $P2_1/n$ with cell parameters: $a = 4.39655(19)$ Å, $b = 13.5720(5)$ Å, $c = 20.0471(5)$ Å, $\beta = 94.753(3)$, $V = 1192.10(7)$ Å^3, $D = 1.683$ g·cm^{-3}, and $Z = 4$. The crystal structure is stabilized by π-π interactions and intermolecular C–H$\cdots$N and C–H$\cdots$O interactions.

1. Introduction

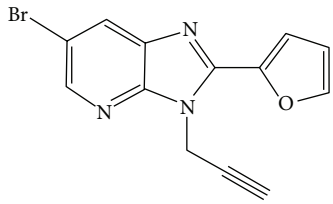
The imidazo[4,5-b]pyridine moiety is an important heterocyclic nucleus having been used extensively in medicinal chemistry. In fact, different compounds derived from this structure have been tested for their potential as anticancer [1], tuberculostatic [2], antimitotic [3], and antineuroinflammatory activities [4].

Due to their great importance, many synthetic strategies have been developed to obtain a variety of substituted structures of this class. The most popular synthetic approach generally involves the cyclocondensation of 2,3-pyridinediamine with carboxylic acid derivatives or with aldehydes [5, 6]. Recently, an ecofriendly synthetic approach including an oxidation in aqueous medium has been claimed [7].

In a previous study, we reacted 6-bromo-2-(furan-2-yl)-3H-imidazo[4,5-b]pyridine with benzyl chloride in the presence of a catalytic quantity of tetra-*n*-butylammonium bromide, under mild conditions, to form 3-benzyl-6-bromo-2-(furan-2-yl)-3H-imidazo[4,5-b]pyridine [8]. In this work, we have synthesized the 3-prop-2-ynyl analogue which is 6-bromo-2-(furan-2-yl)-3-(prop-2-ynyl)-3H-imidazo[4,5-b]pyridine (**1**) (Scheme 1). Owing to the potential biological activities of imidazo[4,5-b]pyridine derivatives, a clear need exists for the preparation of new compounds. In this regard, compound **1** presents some interesting features in the search for new biologically active substances as it contains an additional heterocyclic ring and an alkyne group for easy modification.

2. Material and Methods

6-Bromo-2-furyl-3H-imidazo[4,5-b]pyridine (0.30 g, 1.13 mmoL) was dissolved in DMF (15 mL) and potassium carbonate (0.2 g, 1.48 mmol), and tetra-*n*-butylammonium bromide (0.04 g, 0.1 mmol) and propargyl bromide (0.12 mL, 1.36 mmoL) were then added. Stirring was continued at room temperature for 12 h. The mixture was filtered, and the solvent was removed under reduced pressure. The residue was chromatographed on a column of silica gel with ethyl



Scheme 1: Compound **1**.

acetate-hexane (1/2) as eluent. Compound **1** was obtained as yellow solid.

Single crystals of **1**, $C_{13}H_8BrN_3O$, were crystallized from ethanolic solution. A suitable crystal was selected and measured on an Agilent SuperNova Atlas Dual Source, Agilent Technologies diffractometer using the CrysAlisPro software. The crystal was kept at 199.95(10) K during data collection. Using Olex2 [9], the structure was solved with the SHELXS [10] structure solution program using direct methods and refined with the SHELXL [10] refinement package using least squares minimisation. Nonhydrogen atoms are refined with anisotropic displacement parameters. The molecular connectivity and the crystal packing diagram were drawn using the Mercury (CCDC) program [11] and PyMol [12]. Geometrical calculations were done using Mercury (CCDC) program.

3. Results and Discussion

The details of the crystal data, data collection, and structure refinements are shown in Table 1 and the unique molecule in the crystal structure of **1** in Figure 1.

This compound crystallizes in the monoclinic space group $P2_1/n$ with four molecules in the unit cell. The core heterocyclic structure of the molecule is approximately planar with deviations lower than 0.064 Å from the mean plane. The molecular geometry is stabilized by intermolecular C–H···N and C–H···O interactions which contribute to the stability of the crystal packing (Figure 2). Those interactions involve the relatively acidic hydrogen atom of the terminal alkyne.

An analysis of the crystal packing shows the presence of intermolecular π-π interactions between the imidazole ring and the pyridine ring of two contiguous molecules. This interaction has a 3.635 Å centroid-centroid distance (see Figure 3).

These π-π interactions generate arrays of parallel aromatic subunits along the crystallographic a-direction (Figure 4), while C–H···N and C–H···O interactions form a zigzag structure along the b direction (Figure 5).

A general view of the crystal packing of compound **1** is summarized in Figure 6, where all intermolecular interactions are shown. The arrays formed by π-π interactions along the crystallographic a-direction are shown in green colour. Besides, intermolecular C–H···N and C–H···O interactions are represented with yellow dotted lines providing the generation of a zigzag structure (blue colour) along the b direction.

Table 1: Crystal data and structure refinement for compound **1**.

Empirical formula	$C_{13}H_8BrN_3O$
Formula weight	302.13
Temperature/K	199.95 (10)
Crystal system	Monoclinic
Space group	$P2_1/n$
a/Å	4.39655 (19)
b/Å	13.5720 (5)
c/Å	20.0471 (5)
β/°	94.753 (3)
Volume/Å^3	1192.10 (7)
Z	4
D_{calc} mg/mm^3	1.683
m/mm^{-1}	4.629
F (000)	600.0
Crystal size/mm^3	0.141 × 0.125 × 0.088
2Θ range for data collection	7.88 to 145.74°
Index ranges	$-5 \le h \le 4$, $-16 \le k \le 16$, $-24 \le l \le 24$
Reflections collected	11229
Independent reflections	2362 [R(int) = 0.0455]
Data/restraints/parameters	2362/0/163
Goodness-of-fit on F^2	1.201
Final R indexes [$I \ge 2\sigma(I)$]	R_1 = 0.0389, wR_2 = 0.1052
Final R indexes [all data]	R_1 = 0.0488, wR_2 = 0.1092
Largest diff. peak/hole/e Å^{-3}	0.47/−0.38

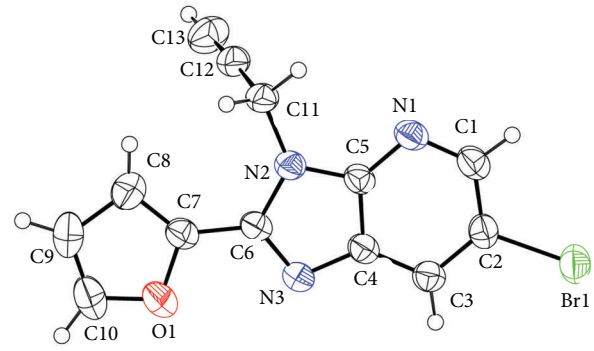


Figure 1: Projection view of **1**.

Tables 2 and 3 summarize the crystallographic data with all bond lengths and bond angles for compound **1**.

4. Conclusions

The compound 6-bromo-2-(furan-2-yl)-3-(prop-2-ynyl)-3H-imidazo[4,5-b]pyridine has been synthesized as a

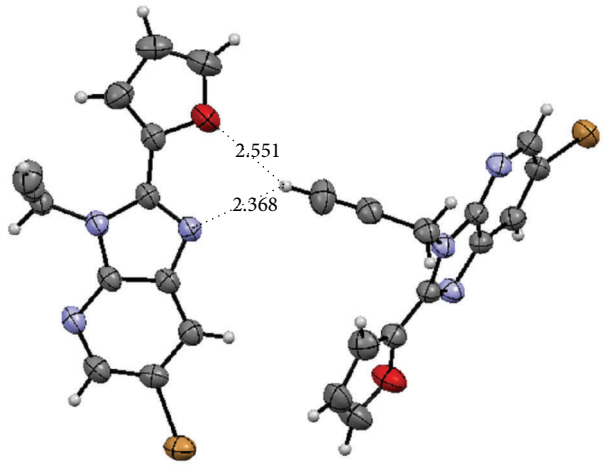


Figure 2: Intermolecular C–H···N and C–H···O interactions for compound **1**.

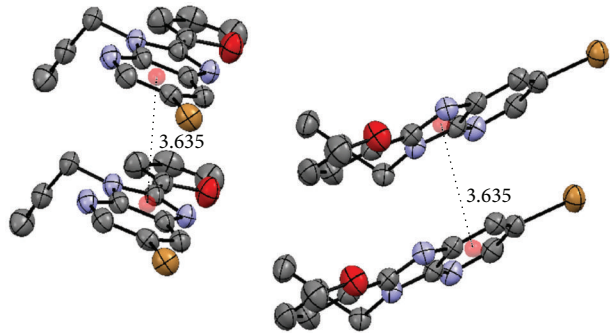


Figure 3: Intermolecular π-π interactions.

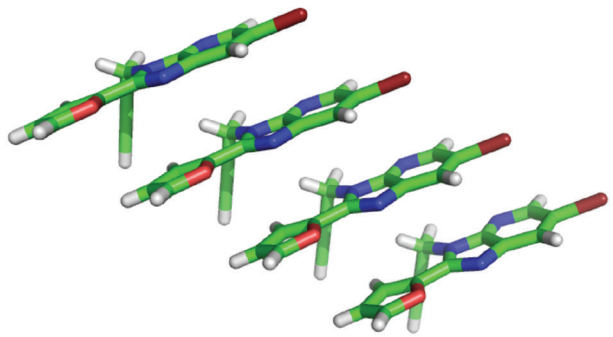


Figure 4: Arrays of parallel aromatic subunits formed by intermolecular π-π interactions.

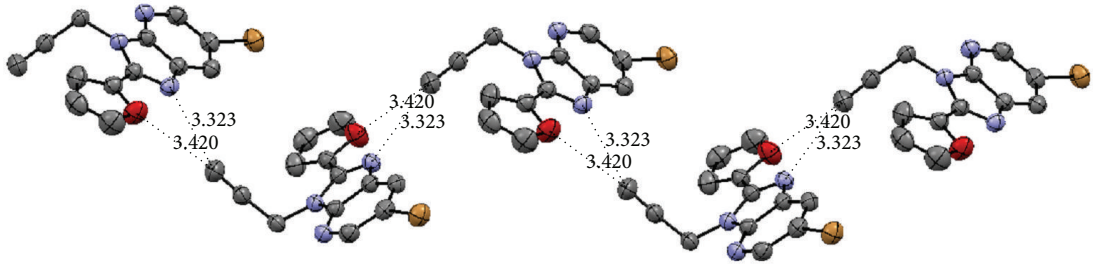


Figure 5: Intermolecular C–H···N and C–H···O interactions forming a zigzag structure along the *b* direction.

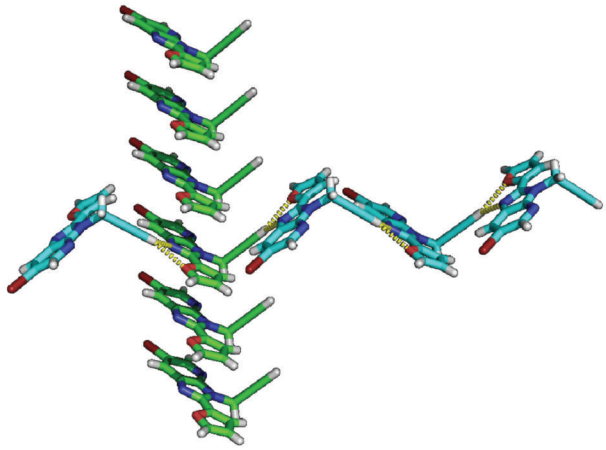


Figure 6: Arrays formed by π-π interactions (green colour) along the crystallographic *a*-direction, and intermolecular C–H···N and C–H···O interactions (showed with yellow dotted lines) forming a zigzag structure (blue colour) along the *b* direction.

Table 2: Bond lengths for compound **1**.

Atom	Atom	Length/Å
Br1	C2	1.894 (3)
C1	C2	1.391 (5)
C1	N1	1.337 (5)
C2	C3	1.386 (5)
C3	C4	1.395 (5)
C4	C5	1.403 (4)
C4	N3	1.379 (4)
C5	N1	1.332 (4)
C5	N2	1.380 (4)
C6	C7	1.445 (5)
C6	N2	1.387 (4)
C6	N3	1.319 (4)
C7	C8	1.340 (5)
C7	O1	1.366 (4)
C8	C9	1.447 (6)
C9	C10	1.307 (6)
C10	O1	1.353 (5)
C11	C12	1.465 (5)
C11	N2	1.462 (4)
C12	C13	1.178 (5)

Table 3: Bond angles for compound **1**.

Atom	Atom	Atom	Angle/°
N1	C1	C2	123.4 (3)
C1	C2	Br1	118.1 (3)
C3	C2	Br1	119.5 (3)
C3	C2	C1	122.3 (3)
C2	C3	C4	115.3 (3)
C3	C4	C5	117.7 (3)
N3	C4	C3	132.0 (3)
N3	C4	C5	110.3 (3)
N1	C5	C4	127.6 (3)
N1	C5	N2	126.6 (3)
N2	C5	C4	105.8 (3)
N2	C6	C7	123.7 (3)
N3	C6	C7	123.2 (3)
N3	C6	N2	113.1 (3)
C8	C7	C6	135.6 (3)
C8	C7	O1	110.6 (3)
O1	C7	C6	113.8 (3)
C7	C8	C9	104.7 (4)
C10	C9	C8	107.3 (4)
C9	C10	O1	110.9 (4)
N2	C11	C12	111.9 (3)
C13	C12	C11	176.4 (4)
C5	N1	C1	113.7 (3)
C5	N2	C6	105.8 (3)
C5	N2	C11	124.4 (3)
C6	N2	C11	129.7 (3)
C6	N3	C4	105.0 (3)
C10	O1	C7	106.4 (3)

new starting material for the development of products with biomedical activities. Its crystal structure has been determined with good precision and accuracy. The molecular structure and crystal packing are stabilized by intermolecular C–H···N and C–H···O hydrogen bonds and intermolecular π-π interactions with the generation of an infinite network.

Acknowledgments

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