



INTERMOLECULAR INTERACTIONS IN MOLECULAR STRUCTURE OF 7-(4-METHOXY-PHENYL)-2,5-DIPHENYL-7H-PYRROLO[2,3-d]PYRIMIDINE-4-YL-AMINE, MONOHYDRATE: X-RAY DIFFRACTION TECHNIQUE

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ABSTRACT

The title molecule, 7-(4-methoxy-phenyl)-2,5-diphenyl-7h-pyrrolo[2,3-d]pyrimidine-4-yl-amine monohydrate ($C_{25}H_{20}N_4O \cdot H_2O$), a novel pyrrolo-pyrimidine derivative crystallizes in a triclinic crystal system in space group $P\bar{1}$ with two molecules per asymmetric unit with two solvent water molecules. Molecular structure is solved with good accuracy with final residual index R converged to 0.097 and goodness of fit $S = 1.053$. Significant number of intermolecular interactions like $N-H...N$, $C-H...O$, $C-H...N$, $\pi...N$ and $C-H...N$ interactions involving all possible donor and acceptor groups contribute to the molecular packing.

Keywords: Pyrrolo-pyrimidine derivative, asymmetric unit, Molecular structure, Residual index.

INTRODUCTION

Pyrrolo-pyrimidine derivatives belong to an important class of N-heterocyclic compounds possessing large biological spectrum like-Antitumor, antiallergic, antiviral, insulin releasing, carbonic anhydrase inhibitory and anti-inflammatory activities [1-6]. In continuation of our interest to work out the three dimensional structures of significant N-heterocyclic derivatives, we report here the molecular structure of 7-(4-methoxy-phenyl)-2,5-diphenyl-7h-pyrrolo[2,3-d]pyrimidine-4-yl-amine, monohydrate (HX3) and the intermolecular interactions involved therein [7-9]. The chemical structure of it, is shown in Figure: 1.

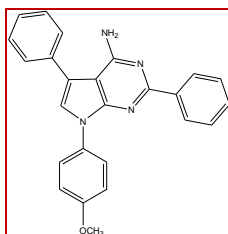


Figure: 1 The chemical structure of the title molecule

METHODOLOGY

The title compound (HX3) has been synthesized by nucleophilic displacement reaction method. Tiny brown diamond like single crystals of it have been grown by slow evaporation method in

toluene. Good diffraction quality single crystals, have been picked up for intensity data collection on single crystal CAD-4 diffractometer using ω -2 θ scan mode with graphite monochromated $MoK\alpha$ radiation ($\lambda=0.71073 \text{ \AA}$) at CSMCRI, Bhavnagar. The preliminary crystallographic data along with data collection details are summarized in Table 1.

Table-1: Preliminary crystallographic data with data collection details

Chemical name	7-(4-methoxy-phenyl)-2,5-diphenyl-7h-pyrrolo[2,3-d]pyrimidine-4-yl-amine, monohydrate
Chemical formula	$C_{25}H_{20}N_4O \cdot H_2O$
Molecular weight	408.45 amu
Crystal system	Triclinic
Space group	$P\bar{1}$
a	9.8892(23) \AA
b	14.4153(34) \AA
c	16.4569(38) \AA
α	78.361(4) $^\circ$
β	74.082(4) $^\circ$
γ	78.049(5) $^\circ$
Volume (V)	2180.81 \AA^3
Z	4 (two molecules per asymmetric unit)
ρ_c	1.244 gm/cm^3
μ	0.081 mm^{-1}
F(000)	856

The structure has been solved using Direct methods and refined by SHELX program [10] built-in within WINGX software program [11]. The final residual index R is 0.097 for 9502 reflections and 561 parameters with goodness of fit S= 1.053. The ORTEP view of the molecule drawn using PLATON software [12], indicating atomic numbering scheme with thermal ellipsoids drawn at 50% probability level is depicted in Figure: 2.

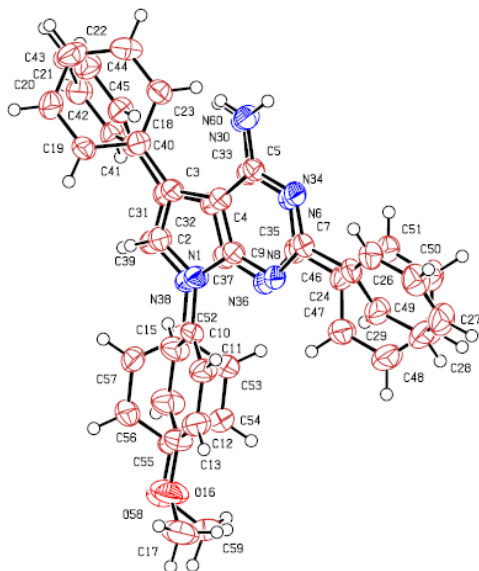


Figure: 2 The ORTEP view of the molecule with two molecules per asymmetric unit

OBSERVATIONS

The title molecule crystallizes in triclinic system with space group $P\bar{1}$ with two molecules in the asymmetric unit alongwith two molecules of solvent water. The fused ring of both the molecules in the asymmetric unit is almost superimposed to each other in the lattice with an angle between two nine membered rings is $2.92(10)^\circ$ in molecule A and $1.45(17)^\circ$ in molecule B.

The selected bond lengths and bond angles involving non-hydrogen atoms are presented in Table 2. The weighted average intra ring torsional angles of the pyrrole and pyridine rings confirmed a planar configuration of the nine membered ring system for both the molecules. The C-N bond lengths in the fused pyrimidine ring vary from $1.331(4)$ to $1.429(4)$

Å, the range of variation agrees reasonably well with literature values for similar structures [13]. The two Nsp²-C bonds: N1-C9 = $1.380(4)$ Å and N1-C2 = $1.381(4)$ Å of the pyrrole ring (Molecule A) and those bonds N38-C37 = $1.374(4)$ Å and N38-C39 = $1.376(4)$ Å in molecule B, are consistent with the reported average value [14].

As normally observed in similar fused derivatives, fusion of the two rings results in significant strain leading to the opening up of the endocyclic angle C4-C9-N8 = $127.2(3)^\circ$ and N6-C7-N8 = $127.2(3)^\circ$ in molecule A and C32-C37-N36 = $127.0(3)^\circ$ and N34-C35-N36 = $126.9(3)^\circ$ in molecule B respectively [15]. The effect is also observed in the exocyclic angles C3-C4-C5 = $138.1(3)^\circ$ and N1-C9-N8 = $124.4(3)^\circ$ of molecule A and C31-C32-C33 = $138.1(3)^\circ$ and N38-C37-N36 = $125.0(3)^\circ$ in molecule B of the fused ring system. Molecular dimensions of benzyl phenyl and the methoxy phenyl ring of both the molecules A and B are normal.

Table-2: Bond lengths (Å) and Bond Angles ($^\circ$) involving non-hydrogen atoms with estimated standard deviation in parentheses

Molecule A		Molecule B	
N1 - C2	1.381(4)	N34 - C35	1.344(4)
N1 - C9	1.380(4)	N34 - C33	1.349(4)
N1 - C10	1.429(4)	N36 - C37	1.334(4)
N6 - C5	1.349(4)	N36 - C35	1.331(4)
N6 - C7	1.334(4)	N38 - C39	1.376(4)
N8 - C7	1.333(4)	N38 - C37	1.374(4)
N8 - C9	1.331(4)	N38 - C52	1.427(4)
O16 - C13	1.379(4)	O58 - C59	1.403(5)
O16 - C17	1.422(6)	O58 - C55	1.361(4)
N30 - C5	1.342(4)	N60 - C33	1.340(4)
C2-N1-C9	107.6(2)	N60-C33-C32	122.2(3)
C2-N1-C10	124.9(3)	N34-C35-N36	126.9(3)
C9-N1-C10	127.3(3)	C35-N36-C37	113.3(3)
C5-N6-C7	118.6(3)	C37-N38-C39	107.7(3)
C7-N8-C9	112.8(3)	C37-N38-C52	126.9(3)
		C39-N38-C52	125.1(3)

RESULTS AND DISCUSSION

Table: 3. Dihedral angles between various least-square planes

Plane	Plane	Angle (°)
1.(N ₁ - C ₂ - C ₃ - C ₄ - C ₉)	2.(C ₄ - C ₅ - N ₆ - C ₇ - N ₈ - C ₉)	3.0(1)
6 (N ₁ - C ₂ - C ₃ - C ₄ - C ₅ - N ₆ - C ₇ - N ₈ - N ₉)	5 (C ₂₄ - C ₂₅ - C ₂₆ - C ₂₇ - C ₂₈ - C ₂₉)	33.8(1)
6 (N ₁ - C ₂ - C ₃ - C ₄ - C ₅ - N ₆ - C ₇ - N ₈ - N ₉)	4 (C ₁₈ - C ₁₉ - C ₂₀ - C ₂₁ - C ₂₂ - C ₂₃)	42.9(1)
6 (N ₁ - C ₂ - C ₃ - C ₄ - C ₅ - N ₆ - C ₇ - N ₈ - N ₉)	3 (C ₁₀ - C ₁₁ - C ₁₂ - C ₁₃ - C ₁₄ - C ₁₅)	38.7(1)
7 (C ₃₁ - C ₃₂ - C ₃₇ - N ₃₈ - C ₃₉)	8 (C ₃₂ - C ₃₃ - N ₃₄ - C ₃₅ - N ₃₆ - C ₃₇)	1.5(1)
12 (C ₃₁ - C ₃₂ - C ₃₃ - N ₃₄ - C ₃₅ - N ₃₆ - C ₃₇ - N ₃₈ - C ₃₉)	11 (C ₅₂ - C ₅₃ - C ₅₄ - C ₅₅ - C ₅₆ - C ₅₇)	41.3(1)
12 (C ₃₁ - C ₃₂ - C ₃₃ - N ₃₄ - C ₃₅ - N ₃₆ - C ₃₇ - N ₃₈ - C ₃₉)	10 (C ₄₆ - C ₄₇ - C ₄₈ - C ₄₉ - C ₅₀ - C ₅₁)	23.27(11)
12 (C ₃₁ - C ₃₂ - C ₃₃ - N ₃₄ - C ₃₅ - N ₃₆ - C ₃₇ - N ₃₈ - C ₃₉)	9 (C ₄₀ - C ₄₁ - C ₄₂ - C ₄₃ - C ₄₄ - C ₄₅)	42.35(08)

All the three phenyl rings of respective molecules are coplanar within themselves (the maximum deviation of the atoms from the respective least-square planes is 0.019(3) Å for benzyl ring 0.008(3) Å for (C10...C15) ring and -0.011(3) Å for (C18-C23) ring). The fused ring system of pyrrole and pyrimidine ring of molecule A is almost planar with dihedral angle of 2.92(17)° and that in molecule B is 1.45(17)°, further confirming the planarity of the fused ring system. The benzyl ring plane (C18....C23) of molecule A and the phenyl ring (C40....C45) of molecule B are almost perpendicular to each other, with dihedral angle of 83.44(11)°, The methyl phenyl ring plane of molecule A is oriented at 78.77(17)° to that of molecule B whereas the phenyl ring plane C₂₄ - C₂₅ - C₂₆ - C₂₇ - C₂₈ - C₂₉ of molecule A lies almost parallel to C₄₆ - C₄₇ - C₄₈ - C₄₉ - C₅₀ - C₅₁ of molecule B with dihedral angle 20.69(18)°. The torsional angles defining molecular conformation are:

C ₉ -N ₁ -C ₁₀ -C ₁₅	-145.4(3)	N ₃₆ -C ₃₅ -C ₄₆ -C ₄₇	-21.7(4)
C ₂ -N ₁ -C ₁₀ -C ₁₁	-137.2(3)	C ₃₉ -C ₃₁ -C ₄₀ -C ₄₅	135.4(3)
C ₃₇ -C ₃₂ -C ₃₃ -N ₃₄	-2.6(4)	C ₄ -C ₃ -C ₁₈ -C ₂₃	45.5(5)

Crystal Packing

The supramolecular structure is mainly stabilized by N-H...N, C-H...N and C-H...O interactions (Figure: 3) along with direction specific π ... π (Figure: 4) and C-H... π interactions (Figure: 5). About half a dozen significant C-H... π interactions involving different moieties contributing to the crystal packing. All these C-H... π interactions are of type III as per the Malone et al, [16] which is the most favourable type of interaction for organic molecule except the C₂₂-H₂₂...C_{g5} interaction which is of type II. The details of these interactions are tabulated in Table 4.

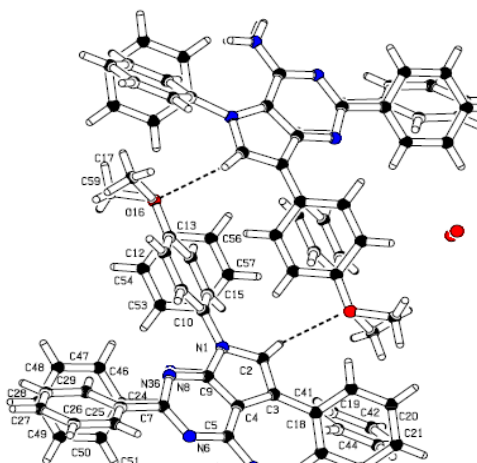


Figure-3: C-H...O interactions in the molecules

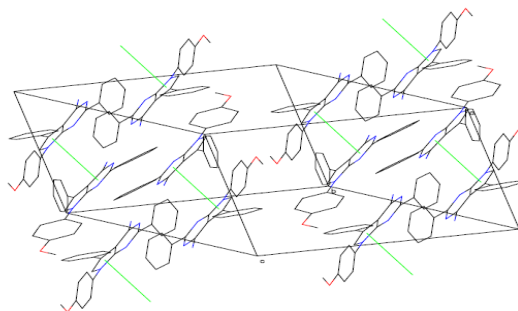


Figure-4: π - π interactions shown with green lines in the packing diagram of molecules

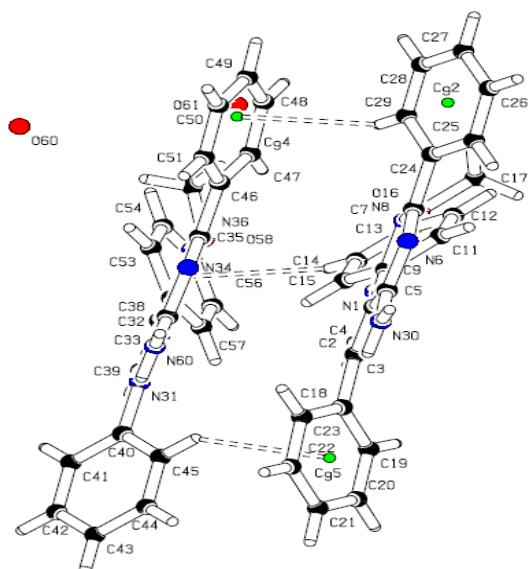


Figure-5: C-H... π interactions shown with double dash lines in the diagram of molecules

Symmetry related molecules are oriented in such a manner that it facilitates intermolecular π ... π interactions and C-H... π interactions. The rare face-to-face π ... π interactions with a dihedral angle of $1.72(17)^\circ$, the distance 3.916 \AA between the ring centroids, the slippage distance 1.056 \AA , are observed and details of it are given in Table 5. The strong conventional N-H...N interactions add its contributions in the molecular packing. Each amine nitrogen N30 and N60 acts as bifurcated donors via H31 and H601 in two strong hydrogen bond interactions with N34 and N6 respectively and also both these amine nitrogen work as acceptor in other two strong interactions with N30 and N60 of symmetry related molecules respectively. There are few more C-H...O and C-H...N interactions, though weak but significant, contributing to the stability of the supramolecular structure, are tabulated in Table 6.

Supplementary Data

The .cif file of this structure has been deposited with Cambridge Crystallographic Data Center as supplementary publication no: CCDC 1572247. Copy of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK.

Table-4: X-H...Cg Interactions

X-H ... Cg	H...Cg (\AA)	X...Cg (\AA)	X- H...C g ($^\circ$)	H \perp	Type
C14-H14...Cg11	2.95	3.706	139	2.82 9	III
C22-H22...Cg5	2.69	3.544	152	2.68 6	II
C25-H25...Cg8	2.95	3.678	136	2.84 5	III
C29-H29...Cg10	2.95	3.694	138	2.80 4	III
C42-H42...Cg4	2.91	3.680	141	2.82 4	III
C45-H45...Cg4	2.98	3.739	140	2.87 9	III
Cg4 = C18 - C19 - C20 - C21 - C22 - C23		Cg5 = C24 - C25 - C26 - C27 - C28 - C29			
Cg8 = C32 - C33 - N34 - C35 - N36 - C37		Cg10 = C46 - C47 - C48 - C49 - C50 - C51			
Cg11 = C52 - C53 - C54 - C55 - C56 - C57					

Table-5: π ... π interactions

Cg(I) Cg (J)	Cg(I)...Cg (J) \AA	Cg... P (\AA)	α	γ	Δ (\AA)
1 8	3.916	3.771	1.72	15.69	1.056

Table-6: Hydrogen bonding interactions

D-H...A	D-H (Å)	H...A (Å)	D...A (Å)	∠D-H...A (°)
N ₃₀ -H ₃₁ -N ₃₄ i	0.860(2)	2.268(2)	3.113(3)	168.05(20)
N ₃₀ -H ₃₁ -N ₆₀ i	0.860(2)	2.933(3)	3.642(4)	141.04(20)
N ₆₀ -H ₆₀₁ -N ₆ i	0.860(2)	2.290(2)	3.123(3)	163.05(20)
N ₆₀ -H ₆₀₁ -N ₃₀ i	0.860(2)	2.945(3)	3.642(4)	139.86(20)
C ₅₁ -H ₅₁ -N ₃₀ i	0.930(3)	2.668(3)	3.430(4)	139.62(22)
C ₂₅ -H ₂₅ -N ₆₀ i	0.930(4)	2.700(3)	3.406(4)	133.39(22)
C ₃₉ -H ₃₉ -O ₅₈ ii	0.930(3)	2.949(2)	3.857(4)	165.73(22)
C ₁₉ -H ₁₉ -O ₅₈ ii	0.930(3)	2.889(3)	3.601(5)	134.39(20)
C ₂₃ -H ₂₃ -N ₆ iii	0.930(3)	2.990(3)	3.895(5)	164.48(21)

Equivalent points

0. x,y,z	i. -x+1,-y+1,-z	ii. -x,-y+1,-z+1
iii. -x,-y+1,-z	iv. x-1,+y,+z	v. -x-1,-y+1,-z+1

CONCLUSION

Molecular orientation of both the molecules A and B in the lattice is such that it facilitates more than dozens of modest to strong varied kind of intermolecular interactions- N-H...N, C-H...O, C-H...N, π ... π and C-H... π interactions resulting in strong molecular stability.

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