International Journal of ChemTech Research
CODEN (USA): IJCRGG ISSN: 0974-4290
Vol.9, No.03 pp 500-505, 2016

Crystal structure analysis of 4-(3-(5-bromo-1H-indol-3-yl)-2-oxoindolin-3-yl)-3-phenylisoxazol-5(2H)-one

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Abstract: The crystal structure of 4-(3-(5-bromo-1H-indol-3-yl)-2-oxoindolin-3-yl)-3-phenylisoxazol-5(2H)-one ($C_{27}H_{22}BrN_3O_4S$). The compound crystallizes in Orthorhombic Pbca space group with unit cell parameters at 296(2) K as follows: a = 14.158(3) Å, b = 14.747(3 8) Å, c = 23.048(7) Å, α = β = γ = 90°. Crystal data were collected using BRUKER SMART APEX II CCD X-ray diffractometer. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares procedures to the final R_1 of 0.089 using SHELXL programs.

Key Words: oxoindoline, isoxazole and crystal structure.

Introduction

Indole containing compounds are best known for their medicinal properties in the pharmaceutical industry. In modern times, analogs based on indole are significant players in a diverse array of markets such as dyes, plastics, agriculture, vitamin supplements, over-the-counterdrugs, flavour enhancers and perfumery[1]. Several indole derivatives, such as sunitinib as tyrosine kinase inhibitor[2] or delavirdine as nonnucleoside reverse transcriptase inhibitor[3], are in clinical use. spiroindole are important heterocyclic compounds with diverse bioactivities[4,5].

Experimental

X-ray Structure Determination

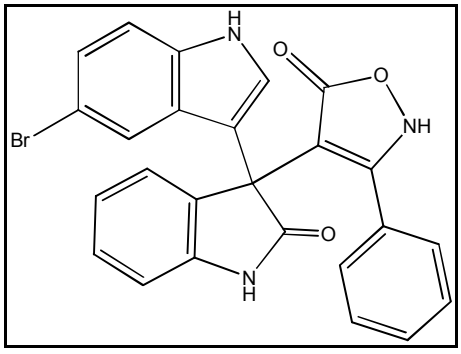
Single crystal of the compound suitable for x-ray diffraction was obtained by slow evaporation method. Three dimensional intensity data were collected on a Bruker[6] SMART APEX CCD Diffractometer using graphite monochromatized Mo-Kα radiation (λ= 0.71073 Å) at Department of chemistry, IIT, Chennai, India. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares procedures using the SHELXL programs[7]. All the non-hydrogen atoms were refined using isotropic and later anisotropic thermal parameters. The hydrogen atoms were included in the structure factor calculation at idealized positions by using a riding model, but not refined. Images were created with ORTEP-3[8]. The crystallographic data for the compound are listed in Table 1.

Table 1: Crystal data and structure refinement of the titled compound

Compound	**Parameters**
Empirical formula	$C_{27}H_{22}BrN_3O_4S$
Formula weight	1128.89
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Pbca
Unit cell dimensions	a = 14.158(3) Å alpha = 90 deg.
	b = 14.747(3) Å beta = 90 deg.
	c = 23.048(7) Å gamma = 90 deg.
Volume	4812(2) $Å^3$
Z, Calculated density	4, 1.558 Mg/m^3
Absorption coefficient	1.836 mm^{-1}
F(000)	2304
Crystal size	0.25 x 0.16 x 0.10 mm
Theta range for data collection	1.77 to 20.90 deg.
Limiting indices	-11<=h<=14, -14<=k<=14, -23<=l<=18
Reflections collected / unique	6282 / 2518 [R(int) = 0.0561]
Completeness to theta = 20.90	98.70%
Max. and min. transmission	0.8377 and 0.6568
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2518 / 0 / 327
Goodness-of-fit on F^2	1.091
Final R indices [I>2sigma(I)]	**R1 = 0.0898**, wR2 = 0.2749
R indices (all data)	R1 = 0.1132, wR2 = 0.2926
Largest diff. peak and hole	0.966 and -0.877 $e.A^{-3}$

Synthesis of the compound

A mixture of 3-(5-bromo-1*H*-indol-3-*yl*)-3-hydroxyindolin-2-one (1 mmol), isoxazolone (1 mmole) and *p*-TSA.H_2O (0.20 mmol) in ethanol (3 mL) was stirred at room temperature for 2 h. The crude compound was purified by column chromatography (5:95 % MeOH/$CHCl_3$) to obtain pure product in good yield (87 %). The purified compound was recrystalised from ethanol and DMSO-D_6 by using slow evaporation method. The scheme diagram is given below.



Results and Discussion

The symmetric unit of the title compound is shown in Fig. 1. The pyrrole ring (N1/C5-C8) is twisted conformation with puckering parameters[9], Q = 0.098 Å and ϕ = 50(7)°. The isoxazole rings O2 and O3 atoms are deviating from the mean plane of (N3-C17-C18-C19) and (N3-O2-C17-C18-C19) by 0.085Å and -0.068Å, respectively. The isoxazole ring is almost orthogonal to the phenyl ring and two indole rings, making a dihedral angle of 34.8(7)°, 3.0(6)° and 74.5(6)°, respectively. The indole ring Br atom are deviating from the mean plane of (N2/C9-C16) -0.093Å.

In the crystal, molecules are linked via N---H...O hydrogen bonds, forms chains along c-axis(Fig 2 & Table 2). The crystal packing is further stabilized by C---H... π and π --- π intermolecular interactions. The selected bond lengths and angles are listed in table 3 and 4, respectively.

Table 2: Hydrogen-bond geometry [Å]

Distance (Å)				**Angle (°)**
D—H…A	D—H	H…A	D…A	D—H…A
N1---H1…O4^{i}	0.86	2.09	2.876(15)	151
N2---H2…O1^{ii}	0.86	2.14	2.949(13)	157
N3---H3…O1^{iii}	0.86	2.16	2.841(14)	136

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

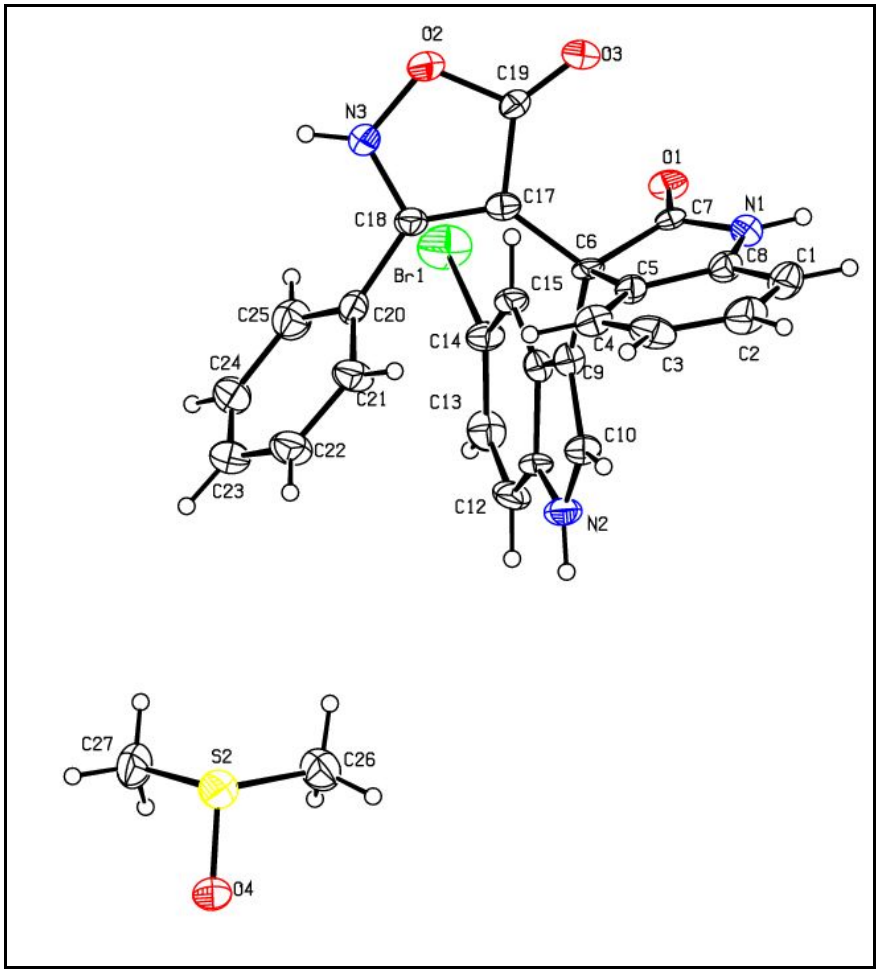


Fig.1. The molecular structure of the title compound, with the atom-numbering scheme. The displacement ellipsoids are drawn at 30% probability level. H atoms are shown as spheres of arbitrary radius.

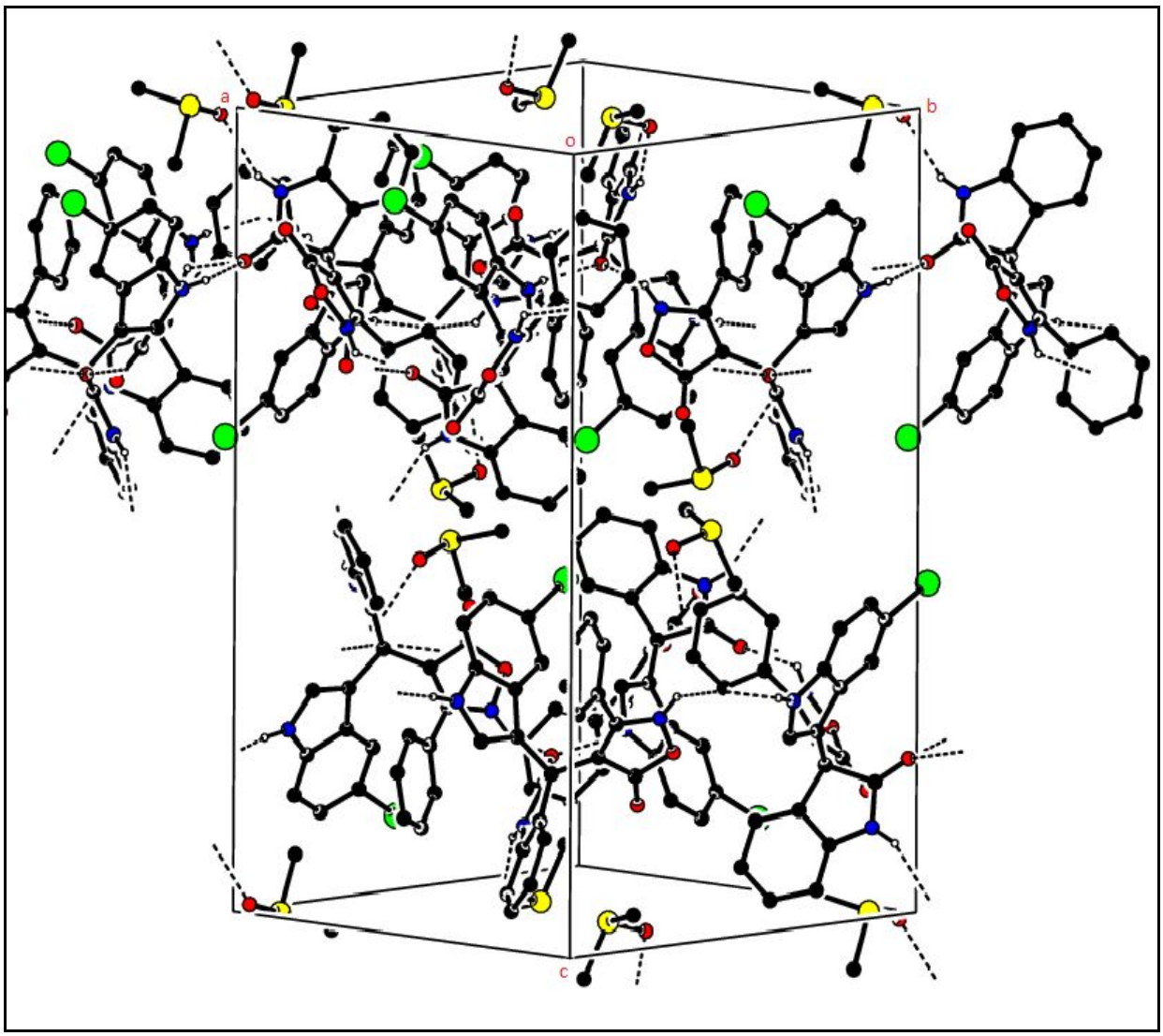


Fig.2. The crystal packing of the title compound, viewed along c axis, showing N---H...O hydrogen bonds. The hydrogen bonds are shown as dashed lines (see Table 2 for details).

Table 3: Selected Bond lengths (Å)

Bond	Length (Å)
N(1)-C(7)	1.369(17)
N(1)-C(8)	1.377(16)
N(1)-H(1)	0.86
N(2)-C(10)	1.351(16)
N(2)-C(11)	1.371(16)
N(2)-H(2)	0.86
N(3)-C(18)	1.348(15)
N(3)-O(2)	1.396(14)
N(3)-H(3)	0.86
O(1)-C(7)	1.206(15)
O(2)-C(19)	1.380(15)
O(3)-C(19)	1.191(15)
Br(1)-C(14)	1.934(12)
C(1)-C(8)	1.366(18)
C(1)-C(2)	1.42(2)
C(1)-H(1A)	0.93
C(2)-C(3)	1.352(19)
C(2)-H(2A)	0.93
C(3)-C(4)	1.398(18)
C(3)-H(3A)	0.93
C(4)-C(5)	1.358(17)
C(4)-H(4)	0.93
C(5)-C(8)	1.386(17)
C(5)-C(6)	1.518(16)
C(6)-C(17)	1.506(16)
C(6)-C(9)	1.526(16)
C(6)-C(7)	1.572(17)
C(9)-C(10)	1.369(17)
C(9)-C(16)	1.441(17)
C(10)-H(10)	0.93

Table 4: Selected Bond angles (º)

Bond	Angle (°)
C(7)-N(1)-C(8)	113.9(11)
C(7)-N(1)-H(1)	123.1
C(8)-N(1)-H(1)	123.1
C(10)-N(2)-C(11)	109.7(10)
C(10)-N(2)-H(2)	125.2
C(11)-N(2)-H(2)	125.2
C(18)-N(3)-O(2)	109.2(10)
C(18)-N(3)-H(3)	125.4
O(2)-N(3)-H(3)	125.4
C(19)-O(2)-N(3)	107.2(9)
C(8)-C(1)-C(2)	116.2(13)
C(8)-C(1)-H(1A)	121.9
C(2)-C(1)-H(1A)	121.9
C(3)-C(2)-C(1)	120.9(12)
C(3)-C(2)-H(2A)	119.6
C(1)-C(2)-H(2A)	119.6
C(2)-C(3)-C(4)	121.2(13)
C(2)-C(3)-H(3A)	119.4
C(4)-C(3)-H(3A)	119.4
C(5)-C(4)-C(3)	118.7(13)
C(5)-C(4)-H(4)	120.6
C(3)-C(4)-H(4)	120.6
C(4)-C(5)-C(8)	119.9(11)
C(4)-C(5)-C(6)	132.2(11)
C(8)-C(5)-C(6)	107.8(10)
C(17)-C(6)-C(5)	115.2(9)
C(17)-C(6)-C(9)	111.4(9)
C(5)-C(6)-C(9)	111.2(8)
C(17)-C(6)-C(7)	109.8(9)
C(5)-C(6)-C(7)	102.6(9)

Conclusion

The crystal structure analysis of a novel oxoindoline and isoxazole compound was studied using x-ray diffraction method. In the crystal, molecules are linked via N---H...O hydrogen bonds, forms chains. The crystal packing is further stabilized by C---H... $\boldsymbol{\pi}$ and $\boldsymbol{\pi}$---$\boldsymbol{\pi}$ intermolecular interactions.

Supplementary Material

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no.CCDC-**1020838**. Copies of available material can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033 or e-mail:deposit@ccdc.cam.ac.uk).

Acknowledgments

The authors thank the Department of chemistry, IIT, Chennai, India, for X-ray intensity data collection.

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