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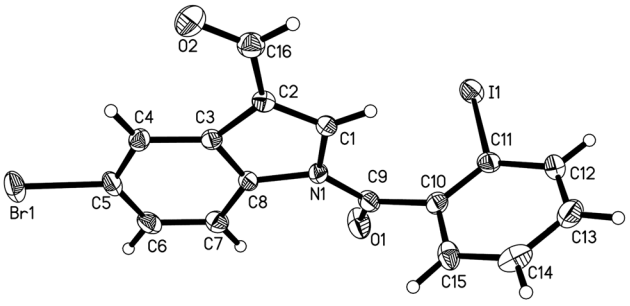
Crystal structure of 5-bromo-1-(2-iodobenzoyl)-1*H*-indole-3-carbaldehyde, $C_{16}H_9BrINO_2$



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Abstract

$C_{16}H_9BrINO_2$, triclinic, $P\bar{1}$ (no. 2), a = 7.9305(12) Å, b = 8.2051(10) Å, c = 11.3141(13) Å, α = 85.384(10)°, β = 85.619(11)°, γ = 87.745(11)°, V = 731.27(17) Å^3, Z = 2, $R_{gt}(F)$ = 0.0397, $wR_{ref}(F^2)$ = 0.0819, T = 293(2) K.

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The crystal structure is shown in figure. Displacement ellipsoids are drawn at the 30 % probability level.

Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

1 Source of material

The title compound 5-bromo-1-(2-iodobenzoyl)-1*H*-indole-3-carbaldehyde was prepared from 5-bromo-1*H*-indole-3-formaldehyde through *N*-acylation reaction. In a dry 25 mL

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.12 × 0.12 × 0.10 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	4.92 mm^{-1}
Diffractometer, scan mode:	SuperNova
θ_{max}, completeness:	25.5°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	4755, 2717, 0.036
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2200
$N(param)_{refined}$:	190
Programs:	CrysAlis^{PRO} [1], SHELX [2, 3]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
Br1	0.05770 (8)	1.02515 (6)	−0.29452 (4)	0.05150 (19)
C1	0.0500 (6)	0.5766 (5)	0.1885 (4)	0.0300 (11)
H1	0.025356	0.500060	0.251976	0.036*
C2	−0.0571 (6)	0.6251 (5)	0.1056 (4)	0.0302 (11)
C3	0.0323 (6)	0.7413 (5)	0.0206 (4)	0.0286 (11)
C4	−0.0112 (6)	0.8206 (5)	−0.0863 (4)	0.0321 (11)
H4	−0.116270	0.810052	−0.115700	0.039*
C5	0.1117 (7)	0.9157 (6)	−0.1458 (4)	0.0367 (13)
C6	0.2685 (7)	0.9356 (6)	−0.1062 (4)	0.0402 (13)
H6	0.345888	1.001913	−0.151113	0.048*
C7	0.3110 (6)	0.8570 (6)	0.0002 (4)	0.0365 (12)
H7	0.415877	0.869423	0.029352	0.044*
C8	0.1899 (6)	0.7584 (5)	0.0622 (4)	0.0288 (11)
C9	0.3337 (6)	0.6401 (6)	0.2417 (4)	0.0351 (12)
C10	0.3341 (6)	0.4842 (6)	0.3209 (4)	0.0349 (12)
C11	0.2931 (6)	0.4771 (6)	0.4414 (4)	0.0350 (12)
C12	0.3017 (6)	0.3305 (6)	0.5105 (5)	0.0429 (14)
H12	0.277281	0.327927	0.592369	0.052*
C13	0.3461 (7)	0.1908 (7)	0.4581 (5)	0.0535 (16)
H13	0.351017	0.091751	0.504058	0.064*
C14	0.3846 (7)	0.1950 (7)	0.3348 (6)	0.0545 (16)
H14	0.410481	0.096925	0.300456	0.065*
C15	0.3855 (6)	0.3344 (6)	0.2643 (5)	0.0405 (13)
H15	0.417242	0.335755	0.183438	0.049*
C16	−0.2265 (7)	0.5685 (6)	0.1017 (5)	0.0407 (13)
H16	−0.264836	0.491862	0.161812	0.049*
I1	0.20158 (4)	0.68494 (4)	0.52463 (3)	0.04539 (15)
N1	0.2014 (5)	0.6546 (4)	0.1677 (3)	0.0286 (9)
O1	0.4414 (5)	0.7402 (5)	0.2382 (3)	0.0526 (10)
O2	−0.3220 (5)	0.6123 (5)	0.0271 (4)	0.0565 (11)

flask, sodium hydride (0.24 g, 6 mmol) was suspended in anhydrous *N,N*-dimethylformamide (DMF, 3 mL) and stirred in an ice water bath for 2 min. Then, a solution composed of 5-methoxy-1*H*-indole-3-formaldehyde (0.26 g, 1.5 mmol) and anhydrous DMF (2 mL) was dropped into the reaction solution and continued to stir for 5 min. Subsequently, 2-iodobenzoyl chloride (0.72 g, 2.7 mmol) dissolved in anhydrous DMF (2 mL) was added dropwise to the reaction solution. After addition, the reaction solution was slowly rose to room temperature and continued stirring for 2 h. Thin-layer chromatography (UV, 254 nm) was used to detect the reaction process. The crude product was dispersed and washed with petroleum ether/ethyl acetate (2:1, *v*/*v*) to obtain a pure product (0.35 g, yield 54.3 %). Single crystals were obtained from *n*-hexane/ethyl acetate (6:1, *v*/*v*) solution.

2 Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, *d* (C–H) = 0.93 Å (aromatic), U_{iso} (H) = 1.2U_{eq} (C).

3 Comment

Nitrogen-containing aromatic heterocycles are common structural fragments in many natural products and drug molecules, and are also useful molecular building blocks in organic synthesis [4, 5]. Among them, indole has attracted much attention due to its unique organic chemical characteristics and biological activities [6, 7]. The most classic reactions of indole included electrophilic reactions at the C(3) position and alkylation or acylation reactions at the N(1) position [8]. Meanwhile, in recent decades, the cross-coupling reactions of indole became a more popular research field [9]. Especially at the C(2) and C(3) positions of indole, due to its high reactivity, it could efficiently couple with olefins or aromatic hydrocarbons to generate a variety of products [10]. In addition, compounds containing indole fragments also exhibited important biological activity. For example, the endogenous active substance 5-hydroxytryptamine, the anti-inflammatory drug indomethacin, and the anti-tumor drug osimertinib contained indole fragments all [11]. On the basis of previous research on the synthesis methodology and pharmaceutical chemistry of indole derivatives, we designed and synthesized a series of compounds with *N*-acyl indole structures, which could serve as key intermediates for synthesizing other anti-inflammatory or anti-tumor active molecules [12].

Single-crystal structure analysis reveals that there is one molecule in the asymmetric unit (*cf*. figure). Bond lengths and angles are within a reasonable range [13–15]. The 5-bromoindole part and iodobenzene part are bridged by a carbonyl group. There is a significant conjugation effect between the carbonyl group and N(1) atom in this molecule, resulting in a significantly shortened bond length for C(9)–N(1) (1.388(6) Å), which is similar to the C–N bonds within the indole ring (1.378(6) Å for C(1)–N(1) and 1.416(6) Å for C(8)–N(1), respectively). The torsion angles of O(1)–C(9)–C(10)–C(11) and O(1)–C(9)–C(10)–C(15) are 75.0(7)° and −103.6(6)° respectively, indicating that the iodobenzene ring and carbonyl group are close to perpendicular. In contrast, the indole ring and carbonyl group are approximately coplanar, because the torsion angles of O(1)–C(9)–N(1)–C(1) and O(1)–C(9)–N(1)–C(8) are −159.3(5)° and 16.1(7)° respectively. In summary, due to the steric hindrance of carbonyl group and iodine atom of this molecule, the indole and iodobenzene rings are not only non-coplanar but nearly perpendicular, with a dihedral angle of approximately 84.7(3)° between them. Moreover, functional groups such as aldehyde, bromine, and iodine provide a wide range of possibilities for this molecule to serve as a key intermediate in the synthesis active compounds.

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