

6-Chloro-2-oxindole: X-ray and DFT-calculated study

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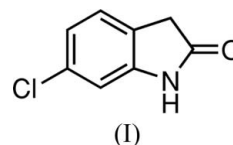
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The molecule of the title compound (systematic name: 6-chloroindolin-2-one), C_8H_6ClNO , is almost planar, with a dihedral angle of $1.13(9)^\circ$ between the planes of the constituent pyrrolidine and benzene rings. Centrosymmetric dimers are formed in the crystal structure by $N-H\cdots O$ hydrogen bonds, and these dimers are additionally linked by $Cl\cdots Cl$ and $C-H\cdots O$ interactions. Density functional theory (DFT) calculations at the B3LYP/6-31 G(d,p) level of theory were used to optimize the molecular structure and the geometry was best reproduced by optimization of two interacting molecules. The bond orders in the molecule, estimated using the natural bond orbitals (NBO) formalism, are consistent with the observed bond lengths. In particular, the contribution of the lone pair of electrons on the N atom to the N—C bond in the N—C=O group is revealed. The measured IR spectrum of the compound shows a red shift of the N—H stretching frequency compared with the free molecule, due to the formation of the hydrogen bonds.

Comment

The structure determination of 6-chloro-2-oxindole, (I), is part of a series of structure determinations of indole derivatives (Hachuła *et al.*, 2008, 2011). There is considerable chemical interest in the development of oxindole derivatives because the heterocyclic ring of oxindole (indolin-2-one) is the basic nucleus of a number of alkaloids (*e.g.* vincatine, mitraphylline, herbaline, crassanine and voachalotin) and of many natural and/or synthetic compounds exhibiting biological and pharmacological activity (Crumeyrolle-Arias *et al.*, 2004; England *et al.*, 2007; Fatima *et al.*, 2007; Galliford & Scheidt, 2007; Peddibhotla, 2009; Midoh *et al.*, 2010). Our interest in the compound comes from investigations of the IR spectra and hydrogen bonding in oxindole (Lipkowski *et al.*, 1995; Hachuła *et al.*, 2011) and in indole derivatives such as indole-3-

carbaldehyde and 3-acetylindole (Flakus *et al.*, 2011; Flakus & Hachuła, 2011).



The molecule of (I) (Fig. 1) is essentially planar (r.m.s. deviation = 0.0149 \AA for all non-H atoms). The dihedral angle between the planes defined by the constituent pyrrolidine and benzene rings is $1.13(9)^\circ$. By comparison, this angle is $4.22(13)^\circ$ in indole-3-carbaldehyde (Ng, 2007) and $0.29(11)^\circ$ in indole-3-carboxylic acid (Smith *et al.*, 2003). The N1—C1 and N1—C8 bond lengths [$1.4006(17)$ and $1.3572(18) \text{ \AA}$, respectively] differ from the corresponding mean values of 1.419 and 1.331 \AA reported for γ -lactams (Allen *et al.*, 1987). Comparable asymmetric bonding patterns are found in similar structures [*e.g.* 3-methylindolin-2-one (Lipkowski *et al.*, 1995),

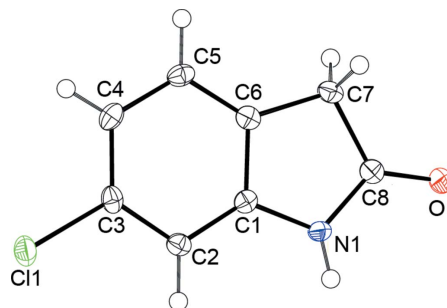


Figure 1

The molecular structure of (I), with displacement ellipsoids drawn at the 50% probability level.

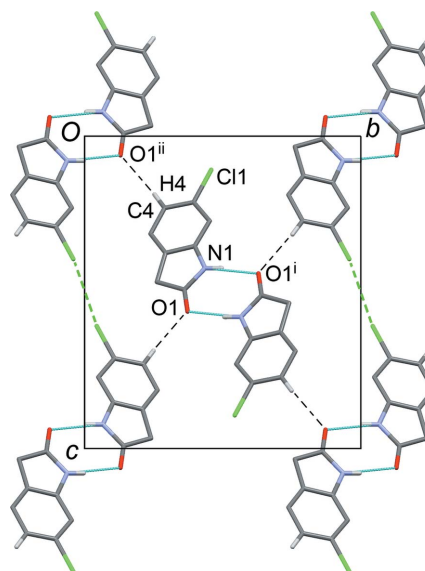


Figure 2

The molecular packing, viewed along the *a* axis, showing dimers formed by $N-H\cdots O$ hydrogen bonds (solid lines), linked by $C-H\cdots O$ (thin dashed lines) and $Cl\cdots Cl$ interactions (thick dashed lines). H atoms not involved in hydrogen bonding have been omitted. (Symmetry codes are as in Table 2.)

3,3-dimethylindolin-2-one (Lipkowski *et al.*, 1995), 3,3-dichloroindolin-2-one (Zukerman-Schpector *et al.*, 1993), 2,3-indolinedione (Bocelli & Grenier-Loustalot, 1982) and 5-hydroxyindolin-2-one (Wei *et al.*, 2004)] and in other indole derivatives [*e.g.* indole-3-carboxaldehyde (Ng, 2007), 3-acetylindole (Hachuła *et al.*, 2008), 3-acetyl-1-methoxyindole (Acheson *et al.*, 1980), indole-3-carboxylic acid (Smith *et al.*, 2003) and indole-3-acetic acid (Karle *et al.*, 1964)]. This is consistent with electron delocalization from the N atom towards the carbonyl group. The C8=O1 bond length [1.2312 (17) Å] is comparable with the mean value of 1.232 Å reported for γ -lactams (Nerskov-Lauritsen *et al.*, 1985). Natural bond orbital (NBO) analysis (Foster & Weinhold, 1980) of the electronic structure [Table 1; showing calculations for a single molecule (*A*) and for a hydrogen-bonded molecular pair (*B*)] confirms that the electrons of the lone pair on atom N1 contribute to the electronic density of the N1—C8 bond, lending it a partial double-bond character.

In the structure of (I), the molecules form dimers across inversion centres through two N—H \cdots O hydrogen bonds (Fig. 2 and Table 2), forming an $R_2^2(8)$ graph-set motif (Etter *et al.*, 1990; Bernstein *et al.*, 1995; Motherwell *et al.*, 1999). According to the hydrogen-bonding classification provided by Steiner (2002) and Desiraju & Steiner (1999), these are medium-strength electrostatic interactions. Neighbouring dimers interact through C4—H4 \cdots O1ⁱⁱ contacts [symmetry code: (ii) $x + 1, -y + \frac{1}{2}, z - \frac{1}{2}$], Cl \cdots Cl interactions [Cl1 \cdots Cl1ⁱⁱⁱ = 3.4378 (6) Å and C3—Cl1 \cdots Cl1ⁱⁱⁱ = 170.87 (5)°; symmetry code: (iii) $-x + 2, -y + 1, -z$] and stacking interactions [interplanar separation of 3.33 (1) Å]. According to the classification of Pedireddi *et al.* (1994), the Cl \cdots Cl contacts are type I in nature, having equal C—Cl \cdots Cl angles.

The experimental values of the bond lengths and angles are in good agreement with those obtained from density functional theory (DFT) calculations (Table 3). The DFT calculations were obtained for both a single molecule (*A*) and a hydrogen-bonded dimer (*B*), comprising two molecules of (I) linked through N—H \cdots O hydrogen bonds. The largest differences between the calculated and experimental values for a single molecule are 0.0332 Å for the bond lengths and 2.0° for the bond angles, while the corresponding values for the hydrogen-bonded dimer are 0.0122 Å and 0.75°. The better agreement in the latter case could be considered as an indication that the intermolecular interactions slightly influence the molecular geometry of (I). The total energy for the geometry-optimized single molecule is -3.918×10^{-15} J and the calculated dipole moment is 1.1904 D. The dipole vector lies in the molecular plane and is oriented approximately along the axis passing through atoms C1 and C4 (Fig. 1). In the structure, the molecular dipoles are arranged antiparallel to each other. The calculated total energy of the two intermolecular hydrogen bonds, corrected for basis-set superposition error (BSSE) using a standard procedure (Boys & Bernardi, 1970), is -81.568 kJ mol⁻¹. The calculated hydrogen-bond geometry (N—H = 1.031 Å, H \cdots O = 1.823 Å, N \cdots O = 2.847 Å and N—H \cdots O = 171.98°) also corresponds well with the experimental data.

In the measured IR spectrum of (I), an intense and broad band in the region 3400–2400 cm⁻¹ can be assigned to the $\nu_{\text{N-H}}$ stretching mode of the N—H group involved in hydrogen bonding. In the IR spectrum derived from the DFT calculations, this band is observed at 3295 cm⁻¹. The shift in the N—H stretch to lower frequency (red shift) compared with the expected non-hydrogen-bonded value of 3451 cm⁻¹ is associated with hydrogen bonding and a lengthening of the N—H bond (Schuster *et al.*, 1976; Schuster & Mikenda, 1999; Jeffrey, 1997). The extent of the shift, $\Delta\nu_s$, is related to important chemical and physical properties, such as hydrogen-bond energy and interatomic distances. For medium-strength hydrogen bonds, the X \cdots A distance ranges from 2.5 to 3.2 Å (X—H *ca.* 1.5–2.2 Å and X—H \cdots A = 130–180°), $\Delta\nu_s$ is expected to be 10–25% and the hydrogen-bond energy lies in the range 4–15 kcal mol⁻¹ (*ca.* 15–60 kJ mol⁻¹; Jeffrey, 1997). Thus, the N—H \cdots O hydrogen bonds in (I) are confirmed to be medium strength. The geometric parameters of (I) are comparable with those of the N—H \cdots O bond occurring in oxindole form II [N \cdots O = 2.833 (2) and 2.857 (2) Å; Hachuła *et al.*, 2011].

Experimental

6-Chloro-2-oxindole (Sigma–Aldrich, 97% pure) was dissolved in acetone and left to evaporate under ambient conditions. Plate-shaped crystals of (I) appeared after a few days. Differential scanning calorimetry of the bulk showed only one sharp endothermic peak at 466.43 K, which corresponds to the melting process. IR (KBr; ν , cm⁻¹): 1700 (*s*) (calculated 1800) $\nu_{\text{C=O}}$; 1622–1002 (*m*) (calculated 1670–1092) $\nu_{\text{C=C}}$ and $\nu_{\text{C-C}}$; 1333 (*m*) (calculated 1332) $\nu_{\text{C-N}}$; 702 (*m*) (calculated 708) $\nu_{\text{C-Cl}}$.

Crystal data

C ₈ H ₆ ClNO	$V = 737.42$ (2) Å ³
$M_r = 167.59$	$Z = 4$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 4.2475$ (1) Å	$\mu = 0.45$ mm ⁻¹
$b = 12.3838$ (2) Å	$T = 100$ K
$c = 14.0372$ (2) Å	$0.60 \times 0.46 \times 0.16$ mm
$\beta = 92.898$ (2)°	

Data collection

Oxford Sapphire3 CCD area-detector diffractometer	4675 measured reflections
Absorption correction: multi-scan (CrysAlis RED; Oxford Diffraction, 2006)	1283 independent reflections
$T_{\text{min}} = 0.775$, $T_{\text{max}} = 0.932$	1203 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.012$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.025$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.068$	
$S = 1.06$	$\Delta\rho_{\text{max}} = 0.21$ e Å ⁻³
1283 reflections	$\Delta\rho_{\text{min}} = -0.25$ e Å ⁻³
104 parameters	

H atoms bound to C atoms were placed in idealized positions and refined as riding, with C—H = 0.95 (aromatic) or 0.99 Å (methylene) and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$. Atom H1 of the NH group was located in a difference Fourier map and refined freely with an isotropic displacement parameter.

Table 1

Wiberg bond orders (WBO; Wiberg, 1968) derived from the natural bond order (NBO) analysis.

	WBO (A)	WBO (B)	WBO (A)	WBO (B)
C1—C3	1.0522	1.0520	C2—C3	1.3850
O1—C8	1.7455	1.6204	C3—C4	1.4179
N1—C8	1.1050	1.1949	C4—C5	1.3978
N1—C1	1.0693	1.0641	C5—C6	1.4452
C1—C2	1.3855	1.3845	C6—C7	1.0174
C1—C6	1.3052	1.3106	C7—C8	0.9667

Table 2

Hydrogen-bond geometry (Å, °).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
N1—H1...O1 ⁱ	0.833 (19)	2.01 (2)	2.8399 (16)	170.4 (17)
C4—H4...O1 ⁱⁱ	0.95	2.39	3.2753 (16)	155

Symmetry codes: (i) $-x, -y + 1, -z + 1$; (ii) $x + 1, -y + \frac{1}{2}, z - \frac{1}{2}$.

DFT calculations were carried out at the B3LYP/6-31G(d,p) level using *GAUSSIAN09* (Parr & Yang, 1989; Frisch *et al.*, 2009), starting from the X-ray geometry. Natural bond orbital calculations (Foster & Weinhold, 1980) were carried out using the program *NBO* (Glendening *et al.*, 1993) included in the *GAUSSIAN09* package.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2006); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2006); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *Mercury* (Macrae *et al.*, 2008); software used to prepare material for publication: *publCIF* (Westrip, 2010).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BI3021). Services for accessing these data are described at the back of the journal.

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Table 3

Comparison of selected geometric data for (I) (Å, °) from calculated (DFT) and X-ray data.

Optimizations are for a single molecule (A) and a hydrogen-bonded dimer (B).

	X-ray	DFT (A)	DFT (B)
C1—C3	1.7523 (14)	1.7597	1.7599
O1—C8	1.2312 (17)	1.2129	1.2303
N1—C8	1.3572 (18)	1.3904	1.3684
N1—C1	1.4006 (17)	1.3975	1.4002
C1—C2	1.3829 (19)	1.3896	1.3896
C1—C6	1.3989 (19)	1.4075	1.4065
C2—C3	1.3921 (19)	1.3991	1.3986
C3—C4	1.385 (2)	1.3933	1.3942
C4—C5	1.398 (2)	1.4024	1.4020
C5—C6	1.3827 (19)	1.3854	1.3856
C6—C7	1.5053 (18)	1.5072	1.5070
C7—C8	1.5219 (19)	1.5394	1.5341
C8—N1—C1	111.65 (12)	112.638	111.793
C2—C1—N1	127.77 (12)	128.503	128.007
C6—C1—N1	109.34 (12)	109.208	109.632
C2—C3—C1	117.84 (11)	118.361	118.436
C4—C3—C1	118.78 (10)	119.154	119.034
C1—C6—C7	108.10 (11)	108.314	107.932
C5—C6—C7	132.56 (12)	132.242	132.494
C6—C7—C8	102.77 (11)	103.711	103.079
O1—C8—N1	125.29 (13)	125.579	126.044
O1—C8—C7	126.59 (12)	128.293	126.392
N1—C8—C7	108.12 (11)	106.128	107.564

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