

4-Benzoyl-3,4-dihydro-2*H*-1,4-benzoxazine-2-carbonitrile: refinement using a multipolar atom modelKrzysztof Ejsmont,<sup>a</sup> Jean-Pierre Joly,<sup>b</sup> Emmanuel Wenger,<sup>c</sup> Benoit Guillot<sup>c</sup> and Christian Jelsch<sup>c\*</sup><sup>a</sup>Faculty of Chemistry, University of Opole, Oleska 48, 45-052 Opole, Poland,<sup>b</sup>UMR 7565 (SRSMC), Structure et Réactivité des Systèmes Moléculaires Complexes, Nancy Université, Faculté des Sciences et Techniques, BP 70239, 54506Vandoeuvre-lès-Nancy Cedex, France, and <sup>c</sup>CNRS UMR 7036 (CRM<sup>2</sup>), Laboratoire de Cristallographie, Résonance Magnétique et Modélisations, Faculté des Sciences et Techniques—UHP, BP 70239, 54506 Vandoeuvre-lès-Nancy Cedex, France

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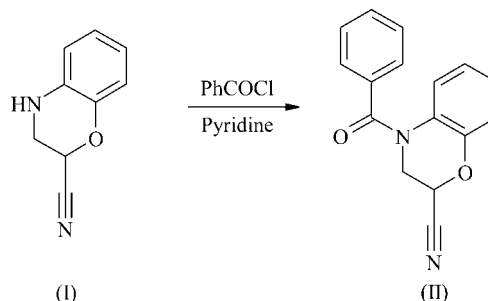
The structural model for the title compound, C<sub>16</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>, was refined using a multipolar atom model transferred from an experimental electron-density database. The refinement showed some improvements of crystallographic statistical indices when compared with a conventional spherical neutral-atom refinement. The title compound adopts a half-chair conformation. The amide N atom lies almost in the plane defined by the three neighbouring C atoms. In the crystal structure, molecules are linked by weak intermolecular C—H···O and C—H···π hydrogen bonds.

## Comment

1,4-Benzoxazines and their derivatives have attracted much attention over the past few decades (Bartsch & Schwarz, 1982). Amongst these systems, cyano-substituted oxazines have been extensively studied (Bartsch & Schwarz, 1983) and cycloaddition reactions with the cyano group reviewed (Myers & Sircar, 1970). More recently, [3+2] cycloadditions of donor–acceptor cyclopropanes and nitriles have found interesting applications in the field of glycal chemistry (Yu & Pagenkopf, 2003). Recently, as part of a more complex 3,4-dihydropyrrole sugar-fused synthesis, we isolated the title *N*-acylated oxine, (II), from known racemic oxine (I) (Bartsch & Schwarz, 1983).

The molecular structure of (II) exists in a half-chair conformation, as depicted with the atomic numbering scheme in Fig. 1. Amide atom N2 is almost exactly in the plane defined by the three neighbouring C atoms (C7, C14 and C15), with all four atoms within 0.05 Å of the plane. The sum of the valence angles around the N atom of 359.7 (2)° demonstrates clear *sp*<sup>2</sup> hybridization (328° for *sp*<sup>3</sup> and 360° for *sp*<sup>2</sup>). The other geometric parameters of (II) (Table 1) are normal and compare well with those found in other crystal structures

(Bartsch & Schwarz, 1983; Black *et al.*, 1987; Garbaskas *et al.*, 1985; Heine *et al.*, 1988; Feng *et al.*, 2007). Compound (II) also exhibits a slight shortening of the amide N—C(=O) bond [1.369 (2) Å], indicative of partial double-bond character; this is typical behaviour for amides.



The crystal structure of (II) is presented in Fig. 2. Molecules of (II) are linked into a three-dimensional framework by three weak C—H···O and a C—H···π hydrogen bond (Table 2).

Initially, in the independent atom model (IAM) refinement, a conventional spherical neutral atom model was applied. Scale factors, atomic positions and displacement parameters for all atoms were refined using the *MOPRO* program (Guillot *et al.*, 2001; Jelsch *et al.*, 2005) until convergence. In the experimental library multipolar atom model (ELMAM) refinement, the same parameters were varied but a multipolar charged atom model was applied. The electron-density parameters were transferred from the ELMAM library (Pichon-Pesme *et al.*, 2004; Zarychta *et al.*, 2007) and subsequently kept fixed. Riding constraints on H-atom isotropic displacement parameters were applied similarly in both refinements, which were carried out with the same diffraction data and using all reflections. The H—X distances were constrained to standard values in neutron diffraction studies (Allen, 1986) in the IAM and ELMAM refinements. The ELMAM refinement shows a slight improvement in statistical indexes when compared with the IAM refinement. The  $I > 2\sigma(I)$  crystallographic factors are reduced from 7.32 to 6.09% for  $R(F)$  and from 2.22 to 2.19% for  $wR(F)$ . The minimum and maximum peaks in the residual electron density are  $-0.095$  and  $0.148$  e Å<sup>-3</sup> after the IAM

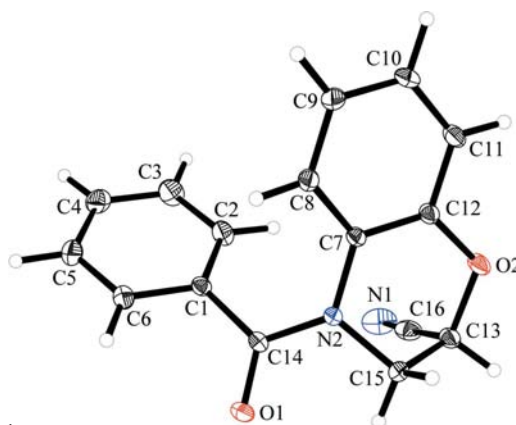
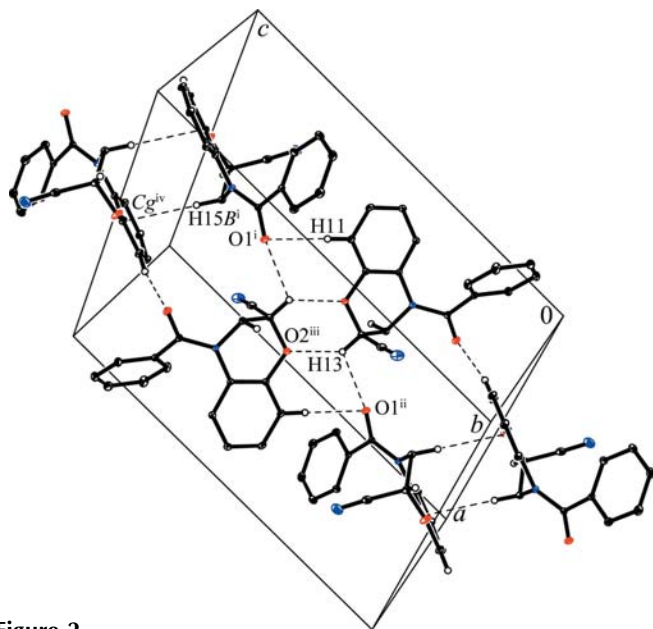


Figure 1

The molecular structure of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.



**Figure 2**

A packing diagram for (II). Dashed lines indicate hydrogen bonds.  $C_g$  is the centroid of the C7–C12 ring. [Symmetry codes: (i)  $x, -y + \frac{1}{2}, z + \frac{1}{2}$ ; (ii)  $-x + 1, y + \frac{1}{2}, -z + \frac{1}{2}$ ; (iii)  $-x + 1, -y + 1, -z + 1$ ; (iv)  $-x + 1, -y, -z + 1$ .]

refinement, and  $-0.103$  and  $0.139 \text{ e } \text{\AA}^{-3}$  after the ELMAM refinement. The improvement is not significant and indicates that the random noise in the residual Fourier map is here larger than the effect of not modelling the bonding electron density.

The largest effect of the multipole transfer on the crystallographic structure is observed for the atomic thermal motion (Jelsch *et al.*, 1998). The average value of  $U_{\text{eq}}$  (geometric mean of eigenvalues  $U_i$ ) derived from the IAM refinement is  $0.0247 \text{ \AA}^2$ , which is slightly higher than the value of  $0.0218 \text{ \AA}^2$  from the ELMAM refinement. The correlation coefficient between both  $U_{\text{eq}}$  sets is only 95%. With the IAM spherical atom model, the displacement parameters are incorrect as they incorporate some significant deformation electron density, due to improper deconvolution between these two features (Jelsch *et al.*, 1998). The transferred multipolar refinement changes the values of the  $U^{ij}$  thermal parameters and improves their accuracy.

When no rigid bond restraints are applied, the r.m.s. of the Hirshfeld (1976) test is  $0.0042 \text{ \AA}^2$  for the spherical atom and  $0.0040 \text{ \AA}^2$  for the multipolar atom model. As the Hirshfeld test was not satisfied, rigid bond restraints were applied in the refinement. The Hirshfeld test may not systematically improve a lot in a multipolar atom refinement compared to a spherical atom model. This is partly because the bonding electron density shared between two atoms is generally located in the middle of the bond and the two  $U^{ij}$  values are similarly perturbed along the bond direction when a spherical atom model is used. Also, the  $U^{ij}$  values may be mainly affected by the errors in the diffraction data which explains the necessity here to use rigid bond restraints even in the multipolar refinement. The improvement of residual electron-density maps, of  $R$  factors and of thermal  $U^{ij}$  parameters is limited in

the case of this structure due to the predominance of errors in the diffraction data *versus* errors in electron-density modelling.

## Experimental

To a solution of racemic secondary amine (I) (Bartsch & Schwarz, 1983) (0.32 g, 2 mmol) in absolute pyridine (25 ml) at 277 K under an argon atmosphere were added benzoyl chloride dropwise (75  $\mu\text{l}$ , 2 equivalents) and 4-(dimethylamino)pyridine (2 mg). The mixture was stirred for 14 h at room temperature and the solvent and reagent excess evaporated under reduced pressure. The residue was dissolved in  $\text{CH}_2\text{Cl}_2$  (50 ml), washed with water ( $3 \times 10 \text{ ml}$ ), isolated, dried over  $\text{MgSO}_4$ , and finally concentrated under reduced pressure. The resulting gum solidified on standing in the dark and was crystallized from hot 96% EtOH to give colourless monocrystals [yield 78%, 0.412 g; m.p. 434–435 K (Tottoli instrument)]. IR (NaCl neat,  $\nu$ ,  $\text{cm}^{-1}$ ): 3056, 2948, 2361, 2350, 2240, 1657, 1495, 1370, 1266;  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.81 (*dd*, 1H,  $J = 2.9$  and 13.9 Hz, H13), 4.74 [*dd*, 1H,  $J = 3.6$  and 13.9 Hz, H15A(B)], 5.3 [*t*, 1H,  $J = 3.3$  and 13.9 Hz, H15B(A)], 6.7–6.8 (*m*, 2H, Ar), 6.95–7.1 (*m*, 2H, Ar), 7.35–7.65 (*m*, 5H, Bz); ES–MS $^+$ : 265.2 (100) [ $M + \text{H}$ ] $^+$ , 238.2 (17) [ $M - \text{CN}$ ] $^+$ . Elemental analysis calculated for  $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$ : C 72.72, H 4.58, N 10.60%; found: C 73.02, H 4.48, N 10.66%.

### Crystal data

$\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$	$V = 1328.06 (11) \text{ \AA}^3$
$M_r = 264.28$	$Z = 4$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 11.8920 (4) \text{ \AA}$	$\mu = 0.09 \text{ mm}^{-1}$
$b = 7.3590 (2) \text{ \AA}$	$T = 100 \text{ K}$
$c = 15.886 (1) \text{ \AA}$	$0.35 \times 0.22 \times 0.17 \text{ mm}$
$\beta = 107.200 (4)^\circ$	

### Data collection

Oxford Diffraction Xcalibur2 diffractometer	$T_{\text{min}} = 0.950$ , $T_{\text{max}} = 1.000$ (expected range = 0.935–0.985)
Absorption correction: multi-scan (CrysAlis RED; Oxford Diffraction, 2008)	53523 measured reflections
	4047 independent reflections
	2724 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.032$

### Refinement

$R[F^2 > 2\sigma(F^2)] = 0.061$	13 restraints
$wR(F) = 0.023$	H-atom parameters constrained
$S = 1.01$	$\Delta\rho_{\text{max}} = 0.14 \text{ e } \text{\AA}^{-3}$
4047 reflections	$\Delta\rho_{\text{min}} = -0.10 \text{ e } \text{\AA}^{-3}$
181 parameters	

Least-squares refinement, based on  $|F|$  using all reflections, was carried out with the program *MOPRO* (Guillot *et al.*, 2001; Jelsch *et al.*, 2005) using the ELMAM electron-density database (Zarychta *et al.*, 2007). No reflection had a negative intensity. The weighted  $R$  factor  $wR$ , conventional  $R$  factor  $R$  and goodness-of-fit  $S$  are based on  $F$ . The threshold expression of  $F^2 > 2\sigma(F^2)$  is used only for calculating  $R(F)$  and is not relevant to the choice of reflections for refinement. The reflection weights were set equal to  $7.29/\sigma^2(F_o)$ . The  $U_{\text{iso}}(\text{H})$  values were constrained to be  $1.2U_{\text{eq}}$  of the parent atom.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2008); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2008); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *MOPRO* (Guillot *et al.*, 2001; Jelsch *et al.*, 2005); molecular graphics:

**Table 1**

Selected geometric parameters (Å, °).

O1—C14	1.227 (1)	N2—C14	1.369 (2)
O2—C12	1.370 (2)	N2—C15	1.470 (2)
O2—C13	1.434 (2)	C13—C16	1.483 (2)
N2—C7	1.424 (2)	N1—C16	1.155 (2)
C7—N2—C14	126.5 (2)	N2—C14—C1	119.6 (1)
C7—N2—C15	113.8 (1)	C13—C16—N1	176.6 (2)
C14—N2—C15	119.4 (1)	C13—C15—N2	107.5 (1)
O1—C14—N2	120.2 (2)	C15—C13—O2	111.7 (1)
O1—C14—C1	119.9 (1)	C16—C13—O2	107.4 (1)
C1—C14—N2—C7	20.9 (1)	C7—C12—O2—C13	9.7 (1)
C1—C14—N2—C15	−152.4 (1)	C12—O2—C13—C16	84.3 (1)
C2—C1—C14—N2	39.2 (1)	C12—O2—C13—C15	−37.9 (1)
C7—N2—C14—O1	−165.0 (1)	C12—C7—N2—C15	26.6 (1)
C7—N2—C15—C13	−52.8 (1)	C13—C15—N2—C14	121.4 (1)
C8—C7—N2—C14	36.6 (1)		

**Table 2**

Hydrogen-bond geometry (Å, °).

*Cg* is the centroid of the C7—C12 ring.

<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>
C11—H11...O1 <sup>i</sup>	1.08	2.31	3.387 (2)	172
C13—H13...O1 <sup>ii</sup>	1.10	2.37	2.902 (2)	108
C13—H13...O2 <sup>iii</sup>	1.10	2.43	3.068 (2)	115
C15—H15B... <i>Cg</i> <sup>iv</sup>	1.09	2.57	3.633 (2)	165

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

*SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *MOPRO*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3197). Services for accessing these data are described at the back of the journal.

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