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# Two (Z)-N-aryl-3-benzylideneisoin-dolin-1-ones

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Two isoindolin-1-one derivatives, (*Z*)-3-benzylidene-*N*-phenylisoindolin-1-one,  $C_{21}H_{15}NO$ , (II), and (*Z*)-3-benzylidene-*N*-(4-methoxyphenyl)isoindolin-1-one,  $C_{22}H_{17}NO_2$ , (III), were synthesized by the palladium-catalysed heteroannulation. The molecules of both compounds have a *Z* configuration. The interplanar angles between the five- and six-membered rings of the isoindolinone moiety in (II) and (III) are 1.66 (11) and 2.26 (7)°, respectively. The phenyl rings at the *N*-position in (II) and (III) are twisted out of the C<sub>4</sub>N ring plane by 62.77 (11) and 67.10 (7)°, respectively. The substitutions at the *N* and C-3 positions of the isoindolinone system have little influence on the molecular dimensions of the resulting compounds.

## Comment

The isoindolinone (phthalimidine) system (I) is present in a number of natural products. Many isoindolinone derivatives display biological activity as potential anti-inflammatory agents, antipsychotics (Zhuang *et al.*, 1998; Linden *et al.*, 1997)



and inhibitors of human CCRF-CEM lymphoblastic leukaemic cells (Taylor *et al.*, 1997). The majority of structurally determined isoindolinone systems are either *N*-substituted or have a hydroxy substituent at the 3-position (Brady *et al.*, 1998; McNab *et al.*, 1997; Barrett *et al.*, 1996; Feeder & Jones, 1996). As part of an ongoing program on the synthesis and characterization of new heterocyclic systems containing an isoindolinone moiety, we have recently reported the crystal structures of several *N* and C-3 substituted derivatives (Khan et al., 1998; Kundu et al., 1999; Guha et al., 1999). The molecular configurations, E or Z, of these compounds are influenced by the type of substituents. To study the effect of



substitution on the conformation of the resulting compounds and to build up a hierarchy for such systems, X-ray analyses of (Z)-3-benzylidene-N-phenylisoindolin-1-one, (II), and (Z)-





The molecular structure of (II) showing the 50% probability displacement ellipsoids.





The molecular structure of (III) showing the 50% probability displacement ellipsoids.

(III), 3-benzylidene-*N*-(*p*-methoxyphenyl)isoindolin-1-one, were undertaken.

The Z configuration of the molecules of (II) and (III), which contain essentially planar isoindolinone and phenyl moieties (see Figs. 1 and 2), are established by the torsion angle N-C14-C15-C16 of 5.4 (5) and 3.3 (4)° in (II) and (III), respectively. The bond lengths and angles observed for the heterocyclic ring in (II) and (III) are similar to those reported for substituted isoindolinone structures (Kundu et al., 1999; Khan et al., 1998; McNab et al., 1997; Feeder & Jones, 1996). The angles between the five- and six-membered rings of the isoindolinone system in (II) and (III) are 1.66 (11) and 2.26  $(7)^{\circ}$ , respectively; the maximum deviation from planarity for an atom in either ring plane is 0.009 (3) Å for C7 in (II), with the carbonyl-O atom 0.030 (3) Å [in (II)] and 0.004 (2) Å [in (III)] away from the C<sub>4</sub>N planes. The phenyl rings (C1-C6) and (C16-C21) in (II) are twisted out of the C<sub>4</sub>N ring plane with dihedral angles 62.77 (11) and 55.72 (10)°, respectively; the corresponding values are 67.10 (7) and 55.05 (7) $^{\circ}$  in (III). In the fused six-membered ring (C8-C13) of (II) and (III), the angles at C9 and C12 are less than 118°, an effect previously noted by McNab et al. (1997). The cis orientation of O2-C22 with respect to C3-C4 about the O2-C3 bond in (III) results in repulsion between the C4 and C22 atoms and because of this the bond angle C4-C3-O2 is increased by about  $9^{\circ}$  (Table 3) compared to C2-C3-O2. The torsion angle C4–C3–O2–C22 is 7.3 (3)°. In both the structures, the carbonyl atoms are involved in weak C-H···O intermolecular contacts (Tables 2 and 4).

A comparison of geometrical parameters of various isoindolinone derivatives (Table 5) reveals that substitutions at Nand/or C-3(C14) positions have apparently little influence on the molecular dimensions. The dihedral angles between the isoindolinone moiety and the planar parts of the R1/R2 groups in different compounds (Table 5) indicate an approximate molecular coplanarity for the N-unsubstituted derivative

Table 1

Table 2

Selected geometric p	arameters (A,	) for (11).	
N-C7	1.395 (3)	C7-C8	1.473 (4)
N-C14	1.421 (3)	C13-C14	1.467 (4)
N-C6	1.423 (3)	C14-C15	1.333 (4)
O-C7	1.216 (3)	C15-C16	1.474 (4)
C7-N-C14	111.4 (2)	C15-C14-N	129.4 (2)
C10-C9-C8	117.5 (3)	C14-C15-C16	130.6 (2)
C11-C12-C13	117.7 (3)		
C6-N-C7-C8	175.7 (3)	N-C14-C15-C16	5.4 (5)
C6-N-C14-C15	6.4 (5)	C13-C14-C15-C16	-173.2 (3)

Intermolecular	$C-H \cdots O$ co	ntacts (Å, <sup>°</sup>	) for	(II).

$D - H \cdot \cdot \cdot A$	$D-{\rm H}$	$H \cdot \cdot \cdot A$	$D \cdots A$	$D - H \cdot \cdot \cdot A$
$C11\!-\!H11\!\cdots\!O^i$	0.93	2.64	3.339 (5)	132.6 (2)
Symmetry code: (i) x	, <i>y</i> , <i>z</i> − 1.			

(Kundu et al., 1999) while the alkyl/aryl substitutions at both the N and C-3 positions introduce considerable puckering in the resulting molecules.

# **Experimental**

2-(2'-Phenylethynyl)-N-phenyl benzamide (PEPB) was synthesized by stirring a mixture of 2-iodo-N-phenyl benzamide (1 mmol) with phenylacetylene (1.2 mmol) in dimethylformamide (DMF) (5 ml) at 353 K for 16 h in the presence of bis(triphenylphosphine)palladium(II) chloride (3.5 mol%), copper iodide (8 mol%) and triethylamine (4 mmol). After usual workup and purification by chromatography (silica gel 60-80 mesh), the product (PEPB) was cyclized to 3-benzylidene-N-phenylisoindolin-1-one, (II), m.p. 470 (1) K, by refluxing with sodium ethoxide in ethanol for 4 h. Single crystals suitable for X-ray analysis were obtained from ethanol. Elemental analysis: calculated for C<sub>21</sub>H<sub>15</sub>NO: C 84.82, H 5.08, N 4.71%; found: C 84.49, H 5.13, N 4.60%. Starting with 2-iodo-N-panisyl benzamide, the procedure as described above yielded 2-(2'phenylethynyl)-N-p-methoxyphenylbenzamide (PEMB), which on cyclization afforded 3-benzylidene-N-(4-methoxyphenyl)isoindolin-1-one, (III), m.p. 441 (1) K. Single crystals suitable for X-ray analysis were obtained from ethanol. Elemental analysis: calculated for C22H17NO2, C 80.91, H 5.23, N 4.27%; found: C 80.90, H 5.36, N 4.13%.

## Compound (II)

C <sub>21</sub> H <sub>15</sub> NO	Cu Ka radiation
$M_r = 297.34$	Cell parameters from 25
Orthorhombic, $P2_12_12_1$	reflections
a = 9.366 (3)  Å	$\theta = 25.1 - 29.8^{\circ}$
b = 19.875(1) Å	$\mu = 0.622 \text{ mm}^{-1}$
c = 8.204 (9)  Å	T = 293 (2)  K
$V = 1527.2 (17) \text{ Å}^3$	Prism, colourless
Z = 4	$0.40 \times 0.30 \times 0.25 \text{ mm}$
$D_x = 1.293 \text{ Mg m}^{-3}$	

## Table 3

Selected geometric parameters (Å, °) for (III).

N-C7	1.400 (3)	O2-C22	1.424 (3)
N-C14	1.417 (3)	C7-C8	1.476 (3)
N-C6	1.432 (3)	C13-C14	1.473 (3)
O1-C7	1.211 (3)	C14-C15	1.340 (3)
O2-C3	1.366 (2)	C15-C16	1.475 (3)
C7 - N - C14	111.9 (2)	$C_{13} - C_{12} - C_{11}$	1180(2)
02 - C3 - C4	124.5(2)	C15 - C14 - N	129.4 (2)
O2-C3-C2	115.5 (2)	C14-C15-C16	131.1 (2)
C10-C9-C8	117.6 (2)		
C6-N-C7-C8	175.9 (2)	N-C14-C15-C16	3.3 (4)
C6-N-C14-C15	4.9 (3)	C13-C14-C15-C16	-176.0 (2)

#### Table 4

Intermolecular  $C-H \cdots O$  contacts for (III).

$D - H \cdots A$	D-H	$H \cdot \cdot \cdot A$	$\cdots A$ $D \cdots A$ $D =$	
$C18-H18\cdots O1^{i}$	0.93	2.58	2.58 3.389 (3) 146.	
Symmetry code: (i) $\frac{1}{2}$ +	$x, \frac{1}{2} - y, \frac{1}{2} + z.$			

Table 5
A comparison of geometrical parameters (Å,°) of substituted isoindolinone compounds.

	R2	Molecular configuration	Torsion angles $N = C = C(R2)$			Dihedral angles			
<i>R</i> 1				C==0	Csp <sup>2</sup> =N	$A^{\wedge}B$	$A^{\wedge}R1$	$A^{\wedge}R2$	Reference
CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	Ζ	-3.1 (2)	1.222 (1)	1.384 (2)-1.412 (2)	0.67 (4)	98.21 (4)	111.11 (4)	(1)
н	C <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub>	Ζ	0.6 (3)	1.225 (2)	1.358 (2)-1.400 (2)	0.79 (6)	- ``	11.91 (6)	(2)
C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	$C(OH)(CH_3)_2$	Ζ	-2.7(8)	1.221 (4)	1.387 (4)-1.417 (4)	0.86 (14)	78.94 (14)	-	(2)
CH <sub>3</sub>	$CO(C_6H_5)$	Ε	177.9 (4)	1.212 (4)	1.388 (5)-1.402 (5)	2.81 (12)	. ,	45.68 (12)	(3)
$C_6H_5$	$C_6H_5$	Ζ	5.4 (5)	1.216 (4)	1.395 (4)-1.421 (3)	1.66 (11)	62.7 (11)	55.72 (10)	(4)
C <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub>	$C_6H_5$	Ζ	3.3 (4)	1.211 (3)	1.400 (3)-1.417 (3)	2.26 (7)	112.90 (7)	55.05 (7)	(4)

† References: (1) Khan et al. (1998); (2) Kundu et al. (1999); (3) Guha et al. (1999); (4) this work.

## Data collection

Rigaku AFC-5*R* diffractometer  $\omega$ -2 $\theta$  scans Absorption correction: empirical (North *et al.*, 1968)  $T_{min} = 0.815, T_{max} = 0.856$ 1589 measured reflections 1589 independent reflections 1403 reflections with  $I > 2\sigma(I)$ 

#### Refinement

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.0436$
$wR(F^2) = 0.1058$
S = 1.116
1589 reflections
208 parameters

## Compound (III)

Crystal data

 $\begin{array}{l} C_{22}H_{17}NO_2\\ M_r = 327.37\\ \text{Monoclinic, } P2_1/n\\ a = 8.577 \ (6) \ \text{\AA}\\ b = 10.542 \ (4) \ \text{\AA}\\ c = 18.272 \ (4) \ \text{\AA}\\ \beta = 98.34 \ (4)^\circ\\ V = 1634.7 \ (13) \ \text{\AA}^3\\ Z = 4 \end{array}$ 

## Data collection

Rigaku AFC-5*R* diffractometer  $\omega$ -2 $\theta$  scans Absorption correction: empirical North *et al.*, 1968  $T_{min} = 0.878$ ,  $T_{max} = 0.934$ 2810 measured reflections 2810 independent reflections 2220 reflections with  $I > 2\sigma(I)$ 

#### Refinement

Refinement on  $F^2$   $R[F^2 > 2\sigma(F^2)] = 0.0483$   $wR(F^2) = 0.1029$  S = 1.0952810 reflections 226 parameters



H-atom parameters constrained  $w = 1/[\sigma^2(F_o^2) + (0.0652P)^2]$ where  $P = (F_o^2 + 2F_c^2)/3$   $(\Delta/\sigma)_{max} = -0.005$   $\Delta\rho_{max} = 0.16 \text{ e} \text{ Å}^{-3}$  $\Delta\rho_{min} = -0.23 \text{ e} \text{ Å}^{-3}$ 

 $D_x = 1.330 \text{ Mg m}^{-3}$ Cu K\alpha radiation Cell parameters from 25 reflections  $\theta = 28.8-39.9^{\circ}$   $\mu = 0.678 \text{ mm}^{-1}$  T = 293 (2) K Prism, colourless  $0.35 \times 0.25 \times 0.10 \text{ mm}$ 

 $\begin{array}{l} \theta_{\max} = 78.92^{\circ} \\ h = 0 \rightarrow 10 \\ k = 0 \rightarrow 13 \\ l = -22 \rightarrow 22 \\ 3 \text{ standard reflections} \\ \text{every 100 reflections} \\ \text{intensity decay: <2%} \end{array}$ 

H-atom parameters constrained  $w = 1/[\sigma^2(F_o^2) + (0.0252P)^2 + 0.5728P]$  where  $P = (F_o^2 + 2F_c^2)/3$   $(\Delta/\sigma)_{max} = -0.004$   $\Delta\rho_{max} = 0.15 \text{ e } \text{\AA}^{-3}$  $\Delta\rho_{min} = -0.15 \text{ e } \text{\AA}^{-3}$ 

All H-atoms were generated using *HFIX* in *SHELX*93 (Sheldrick, 1993).  $U_{\rm iso}$  for H atoms were assigned as 1.2 times  $U_{\rm eq}$  of the parent non-H atoms before anisotropic refinement.

For both compounds, data collection: MSC/AFC Diffractometer Control Software (Molecular Structure Corporation, 1993); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1995); program(s) used to solve structure: *MULTAN*88 (Debaerdemaeker *et al.*, 1988); program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *ZORTEP* (Zsolnai, 1995); software used to prepare material for publication: *SHELXL*93 and *PARST* (Nardelli, 1995).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1206). Services for accessing these data are described at the back of the journal.

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