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Two (*Z*)-*N*-aryl-3-benzylideneisoindolin-1-ones

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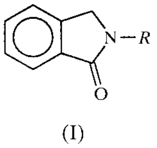
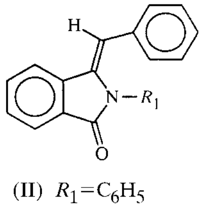
Two isoindolin-1-one derivatives, (*Z*)-3-benzylidene-*N*-phenylisoindolin-1-one, $C_{21}H_{15}NO$, (II), and (*Z*)-3-benzylidene-*N*-(4-methoxyphenyl)isoindolin-1-one, $C_{22}H_{17}NO_2$, (III), were synthesized by the palladium-catalysed heteroannulation. The molecules of both compounds have a *Z* 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_4N 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

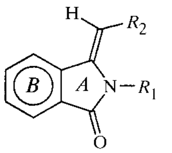


(I)



(II) R_1=C_6H_5
(III) R_1=C_6H_4OMe

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*)-



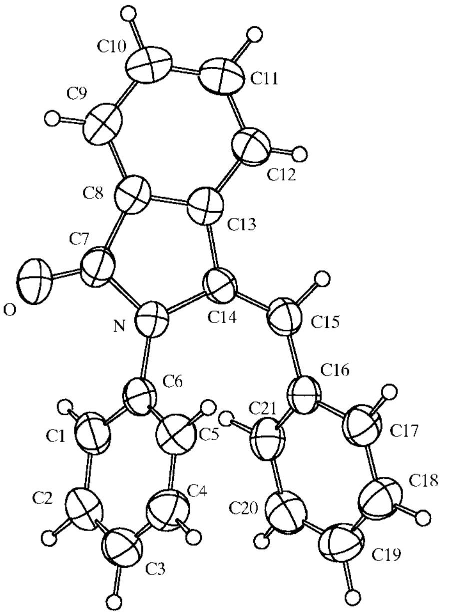


Figure 1
The molecular structure of (II) showing the 50% probability displacement ellipsoids.

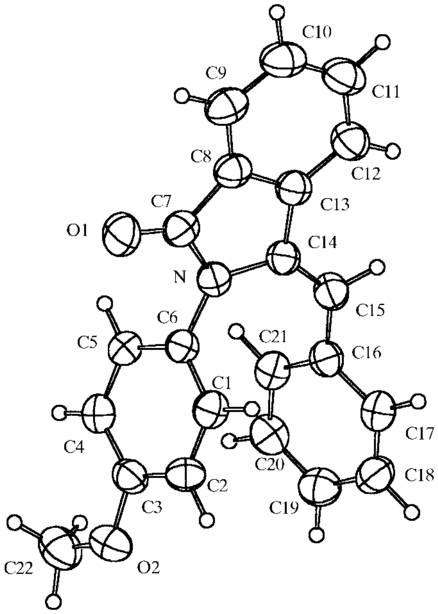


Figure 2
The molecular structure of (III) showing the 50% probability displacement ellipsoids.

3-benzylidene-*N*-(*p*-methoxyphenyl)isoindolin-1-one, (III), 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)°, 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_4N planes. The phenyl rings (C1—C6) and (C16—C21) in (II) are twisted out of the C_4N ring plane with dihedral angles 62.77 (11) and 55.72 (10)°, respectively; the corresponding values are 67.10 (7) and 55.05 (7)° 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° (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 *N* and/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 *R*1/*R*2 groups in different compounds (Table 5) indicate an approximate molecular coplanarity for the *N*-unsubstituted derivative (Kundu *et al.*, 1999) while the alkyl/aryl substitutions at both the *N* and C-3 positions introduce considerable puckering in the resulting molecules.

Table 1
Selected geometric parameters (Å, °) for (II).

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)

Table 2
Intermolecular C—H···O contacts (Å, °) for (II).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C11—H11···O^i	0.93	2.64	3.339 (5)	132.6 (2)

Symmetry code: (i) $x, y, z-1$.

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 $C_{21}H_{15}NO$: C 84.82, H 5.08, N 4.71%; found: C 84.49, H 5.13, N 4.60%. Starting with 2-iodo-*N*-*p*-anisyl 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 $C_{22}H_{17}NO_2$, C 80.91, H 5.23, N 4.27%; found: C 80.90, H 5.36, N 4.13%.

Compound (II)

Crystal data

$C_{21}H_{15}NO$	Cu $K\alpha$ radiation
$M_r = 297.34$	Cell parameters from 25 reflections
Orthorhombic, $P2_12_12_1$	$\theta = 25.1–29.8°$
$a = 9.366 (3)$ Å	$\mu = 0.622$ mm^{-1}
$b = 19.875 (1)$ Å	$T = 293 (2)$ K
$c = 8.204 (9)$ Å	Prism, colourless
$V = 1527.2 (17)$ Å^3	0.40 × 0.30 × 0.25 mm
$Z = 4$	
$D_x = 1.293$ 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)	C13—C12—C11	118.0 (2)
O2—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···O contacts for (III).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C18—H18···O1^i	0.93	2.58	3.389 (3)	146.4 (1)

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.

*R*1	*R*2	Molecular configuration	Torsion angles N═C═C═C(*R*2)	C═O	C*sp*²═N	Dihedral angles *A*^*B*	 *A*^*R*1	 *A*^*R*2	Reference
$CH_2C_6H_5$	C_6H_5	*Z*	−3.1 (2)	1.222 (1)	1.384 (2)–1.412 (2)	0.67 (4)	98.21 (4)	111.11 (4)	(1)
H	$C_6H_4OCH_3$	*Z*	0.6 (3)	1.225 (2)	1.358 (2)–1.400 (2)	0.79 (6)	–	11.91 (6)	(2)
$C_6H_4CH_3$	$C(OH)(CH_3)_2$	*Z*	−2.7 (8)	1.221 (4)	1.387 (4)–1.417 (4)	0.86 (14)	78.94 (14)	–	(2)
CH_3	$CO(C_6H_5)$	*E*	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	*Z*	5.4 (5)	1.216 (4)	1.395 (4)–1.421 (3)	1.66 (11)	62.7 (11)	55.72 (10)	(4)
$C_6H_4OCH_3$	C_6H_5	*Z*	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
ω–2θ scans
Absorption correction: empirical (North *et al.*, 1968)
$T_{\rm min} = 0.815$, $T_{\rm max} = 0.856$
1589 measured reflections
1589 independent reflections
1403 reflections with $I > 2\sigma(I)$

$\theta_{\rm max} = 79.70°$
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 23$
$l = 0 \rightarrow 10$
3 standard reflections every 100 reflections intensity decay: <2%

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

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

Compound (III)

Crystal data

$C_{22}H_{17}NO_2$
$M_r = 327.37$
Monoclinic, $P2_1/n$
$a = 8.577$ (6) Å
$b = 10.542$ (4) Å
$c = 18.272$ (4) Å
$\beta = 98.34$ (4)°
$V = 1634.7$ (13) Å^3
$Z = 4$

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

Data collection

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

$\theta_{\rm max} = 78.92°$
$h = 0 \rightarrow 10$
$k = 0 \rightarrow 13$
$l = -22 \rightarrow 22$
3 standard reflections every 100 reflections intensity decay: <2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0483$
$wR(F^2) = 0.1029$
$S = 1.095$
2810 reflections
226 parameters

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