Isatin 3-semicarbazone and 1-methylisatin 3-semicarbazone

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The two title semicarbazones, namely 2,3-dihydro-1H-indole-2,3-dione 3-semicarbazone, $C_9H_8N_4O_2$, (I), and 1-methyl-2,3-dihydro-1H-indole-2,3-dione 3-semicarbazone, $C_{10}H_{10}N_4O_2$, (II), show the same configuration, viz. Z around the imine C=N bond and E around the C(O)—NH$_2$ bond, stabilized by two intramolecular hydrogen bonds. The presence of a methyl group on the isatin N atom determines the difference in the packing; in (I), the molecules are linked into chains which lie in the crystallographic (102) plane and run perpendicular to the b axis, while in (II), the molecules are arranged to form helices running parallel to a crystallographic screw axis in the a direction.

Comment

Isatin derivatives are molecules that possess biological properties (Pandeya et al., 1999, and references therein). During the past few years, we have devoted our research to isatin derivatives and their metal complexes in order to study their biological activity (Rodríguez-Argüelles et al., 1999, 2004; Casas et al., 2000). In this framework, we report here the synthesis and solid-state characterization of two semicarbazones, viz. isatin and 1-methylisatin 3-semicarbazone, denoted (I) and (II), respectively.
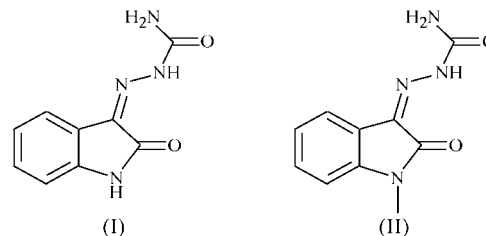
The configuration of (I) (Fig. 1) is Z with respect to the C2—N3 bond (with the configuration stabilized by an intramolecular N2—H3···O2 hydrogen bond; Table 2), while it is E with respect to the C1—N2 bond (stabilized by an intramolecular N1—H2···N3 hydrogen bond; Table 2). The same configurations have been found in uncomplexed isatin 3-thiosemicarbazone (Casas et al., 2000) and in isatin thio-
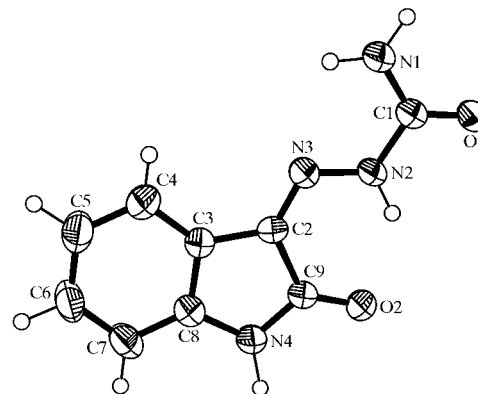

Figure 1
An ORTEPIII (Burnett & Johnson, 1996) view of the molecule of (I), with displacement ellipsoids drawn at the 50% probability level.

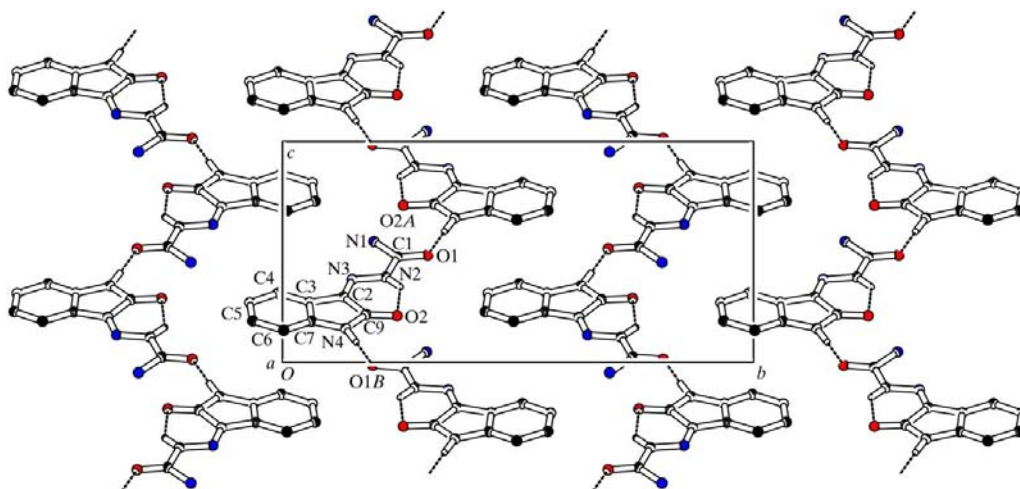**Figure 2**
A packing diagram for (I), with hydrogen bonds indicated by dashed lines. Suffixes A and B correspond to the symmetry codes (i) and (ii) in Table 2.

organic compounds

semicarbazone ethyl or *p*-tolyl monosubstituted on the amine N atom (Bain *et al.*, 1997; Revenko *et al.*, 1994). The bond distances and angles are listed in Table 1 and are comparable to those reported in the literature for similar compounds (Allen, 2002). In the five-membered ring, the C2—C9 bond [1.505 (3) Å] is shorter than the corresponding bond in free isatin [1.555 (3) Å; Palenik *et al.*, 1990]. This difference confirms the hypothesis that the bond lengthening of unsubstituted isatin is due to repulsion between the lone pair of the O atom in the *cis* position. The six- and five-membered rings are nearly planar [the dihedral angle between the mean planes of the two rings is 1.20 (6)°], and the dihedral angle between the mean planes of the isatin and semicarbazide groups is 5.42 (5)°. These molecules could take the keto–imine tautomeric form in solution, but in the crystal only the keto form is observed, as confirmed by the C9=O2 distance [1.230 (2) Å]. This form is stabilized by intermolecular hydrogen bonding (i) between amine atom N1 and atom O2 at $(x - 1, -y + \frac{1}{2}, z + \frac{1}{2})$ and (ii) between isatin atom N4 and atom O1 of the semicarbazide moiety at $(x + 1, -y + \frac{1}{2}, z - \frac{1}{2})$ (Table 2). This short hydrogen bond justifies the unusually long N4—H8 distance (1.04 Å). These two bonds l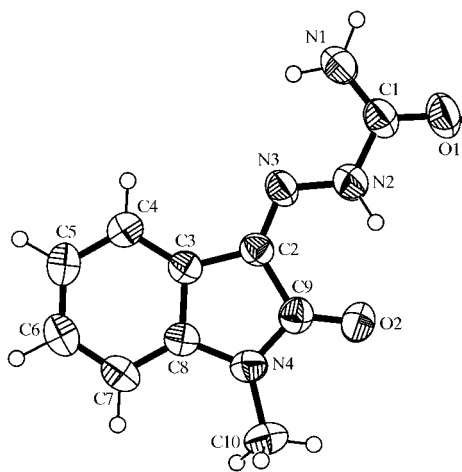ink the molecules into chains lying in the crystallographic (102) plane and running perpendicular to the *b* axis (Fig. 2). Forces that can probably be interpreted as due to stacking interactions between the six-membered rings of centrosymmetric molecules (in the range 3.340–3.519 Å) hold the chains together to form a complex network in the *c* and *a* directions.

Fig. 3 shows an *ORTEPIII* (Burnett & Johnson, 1996) view of (II). The molecular geometry is similar to that of the non-methylated compound (I). The configuration is *Z* around the C2—N3 bond, stabilized by an intramolecular N2—H3···O2 bond, and *E* with respect to the C1—N2 bond as a consequence of an intramolecular N1—H2···N3 bond (Table 3). Again, the C2—C9 bond [1.497 (3) Å] is shorter than that in free isatin. The dihedral angle between the mean planes of the two rings is 1.04 (9)°, and that between the mean planes of the isatin and semicarbazide groups is 1.61 (9)°. The whole molecule is therefore essentially planar. In the crystal packing (Fig. 4), which is different from that of (I), the presence of hydrogen bonds between atoms N1 and O1 of molecules related by a 2_1 axis (Table 3) gives rise to a helix running parallel to the crystallographic *a* axis. Weak C—H···O interactions between an aromatic isatin C atom, a methyl C atom and a carbonyl O atom are also present (see Table 3 for details).

Figure 3
An *ORTEPIII* (Burnett & Johnson, 1996) view of the molecule of (II), with displacement ellipsoids drawn at the 50% probability level.

Experimental

The title compounds were obtained from isatin or 1-methylisatin and neutral semicarbazide (1:1 molar ratio) in an ethanol–water solution, following a similar procedure to that reported by Tomchin *et al.* (1973). The solids obtained on cooling were filtered off, washed with 98% ethanol and dried in a vacuum. For isatin 3-semicarbazone, $H_2L^1 \cdot H_2O$: yellow powder, solid, m.p. 564 K; analysis found: C 48.8, H 4.4, N 25.0%; calculated for $C_9H_8N_4O_2 \cdot H_2O$: C 48.7, H 4.5, N 25.2%; yield 54%. The solid was dissolved in ethyl acetate and after several days at room temperature the solution afforded crystals of (I) that were extremely small but suitable for X-ray diffraction studies and that did not contain the water molecule observed for the powder. For 1-methylisatin 3-semicarbazone, HL^2: yellow solid, m.p. 522 K; analysis found: C 54.9, H 4.7, N 25.0%; calculated for $C_{10}H_{10}N_4O_2$: C 55.0, H 4.6, N 25.7%; yield 57%. After several days at room temperature, the solution afforded crystals of (II) that were suitable for X-ray diffraction studies.
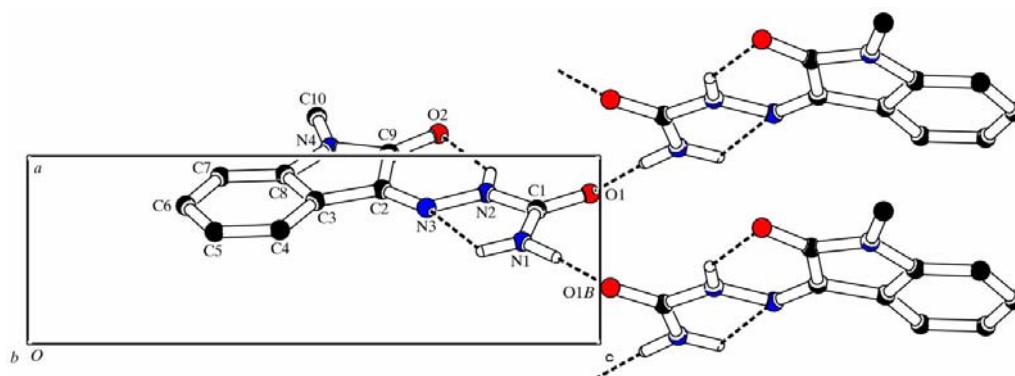

Figure 4
A packing diagram for (II), with hydrogen bonds indicated by dashed lines. The suffix *B* corresponds to symmetry code (iii) in Table 3.

Compound (I)

Crystal data

$C_9H_8N_4O_2$
$M_r = 204.19$
Monoclinic, $P2_1/c$
$a = 5.554 (1)$ Å
$b = 18.754 (3)$ Å
$c = 8.974 (2)$ Å
$\beta = 101.84 (3)°$
$V = 914.8 (3)$ Å^3
$Z = 4$
$D_x = 1.483$ Mg m^{-3}

Cu $K\alpha$ radiation
Cell parameters from 20 reflections
$\theta = 20–30°$
$\mu = 0.93$ mm^{-1}
$T = 298 (2)$ K
Prism, pale yellow
$0.3 \times 0.2 \times 0.2$ mm

Data collection

Siemens AED diffractometer
θ–2θ scans
1438 measured reflections
1354 independent reflections
907 reflections with $I > 2\sigma(I)$
$R_{int} = 0.032$
$\theta_{max} = 62.5°$

$h = -6 \rightarrow 5$
$k = 0 \rightarrow 21$
$l = 0 \rightarrow 10$
1 standard reflection
  every 100 reflections
  intensity decay: 1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.092$
$S = 0.93$
1354 reflections
136 parameters

H-atom parameters not refined
$w = 1/[\sigma^2(F_o^2) + (0.0504P)^2]$
  where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.013$
$\Delta\rho_{max} = 0.17$ e Å^{-3}
$\Delta\rho_{min} = -0.15$ e Å^{-3}

Table 1
Selected interatomic distances (Å) for (I).

O1—C1	1.224 (2)	C2—C3	1.454 (3)
O2—C9	1.230 (2)	C2—C9	1.505 (3)
N1—C1	1.336 (3)	C3—C4	1.383 (3)
N2—N3	1.356 (2)	C3—C8	1.395 (3)
N2—C1	1.380 (3)	C4—C5	1.380 (3)
N3—C2	1.293 (3)	C5—C6	1.384 (4)
N4—C9	1.355 (3)	C6—C7	1.380 (3)
N4—C8	1.411 (2)	C7—C8	1.372 (3)

Table 2
Hydrogen-bond geometry (Å, °) for (I).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1$\cdots$O2^i	0.91	2.18	3.087 (3)	173
N1—H2$\cdots$N3	0.94	2.25	2.659 (3)	106
N2—H3$\cdots$O2	0.93	2.00	2.755 (2)	137
N4—H8$\cdots$O1^{ii}	1.04	1.74	2.777 (2)	178

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

Compound (II)

Crystal data

$C_{10}H_{10}N_4O_2$
$M_r = 218.22$
Orthorhombic, $P2_12_12_1$
$a = 3.984 (2)$ Å
$b = 20.930 (6)$ Å
$c = 12.122 (2)$ Å
$V = 1010.8 (6)$ Å^3
$Z = 4$
$D_x = 1.434$ Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 3118 reflections
$\theta = 2.1–25.0°$
$\mu = 0.11$ mm^{-1}
$T = 298 (2)$ K
Prism, yellow
$0.4 \times 0.3 \times 0.2$ mm

Data collection

Bruker SMART 1000 diffractometer
ω scans
Absorption correction: multi-scan (SADABS; Bruker, 1999)
  $T_{min} = 0.939, T_{max} = 0.980$
9231 measured reflections

1463 independent reflections
1242 reflections with $I > 2\sigma(I)$
$R_{int} = 0.038$
$\theta_{max} = 25.0°$
$h = -4 \rightarrow 4$
$k = -23 \rightarrow 23$
$l = -13 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.028$
$wR(F^2) = 0.069$
$S = 1.00$
1463 reflections
145 parameters

H-atom parameters not refined
$w = 1/[\sigma^2(F_o^2) + (0.0416P)^2]$
  where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.003$
$\Delta\rho_{max} = 0.10$ e Å^{-3}
$\Delta\rho_{min} = -0.11$ e Å^{-3}

Table 3
Hydrogen-bond geometry (Å, °) for (II).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1$\cdots$O1^{iii}	0.99 (2)	1.92 (2)	2.898 (3)	170 (2)
N1—H2$\cdots$N3	0.89 (2)	2.25 (2)	2.654 (3)	107 (2)
N2—H3$\cdots$O2	0.94 (2)	1.95 (2)	2.741 (3)	140 (2)
C7—H7$\cdots$O2^{iv}	1.01 (2)	2.41 (2)	3.376 (3)	160 (2)
C10—H10$C\cdots$O2	0.96	2.55	2.906 (3)	102

Symmetry codes: (iii) $x - \frac{1}{2}, -y + \frac{1}{2}, -z + 2$; (iv) $-x + \frac{5}{2}, -y, z - \frac{1}{2}$.

In (I), all H atoms were located in a difference map, except for aromatic atoms H4 and H7, which were calculated with standard geometries. In (II), all atoms were visible in difference maps and were subsequently allowed for as riding atoms, with C—H = 0.93–0.96 Å, N—H = 0.86 Å and $U_{iso}(H) = 1.2U_{eq}(C,N)$, or $1.5U_{eq}(C)$ for the methyl groups. In the absense of significant anomalous scattering in (II), the Flack (1983) parameter was indeterminate (Flack & Bernardinelli, 2000), and the Friedel-equivalent reflections were merged prior to the final refinements.

For (I), data collection: local program (Belletti *et al.*, 1988); cell refinement: local program (Belletti *et al.*, 1988); data reduction: local program (Belletti *et al.*, 1988). For (II), data collection: *SMART* (Bruker, 1999); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1999). For both compounds, program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPIII* (Burnett & Johnson, 1996) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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