(2RS)-3-(4-Hydroxyphenyl)-2-(1-oxo-1H-2,3-dihydroisoindol-2-yl)propanoic acid monohydrate

John F. Gallagher and Fiona Brady
Compound (I) (derived from dl-tyrosine) crystallizes as a hydrogen-bonded acid–monohydrate dimer (with molecules A/B, O1W, O2W positioned to maximize hydrogen bonding within the asymmetric unit); this is depicted with the atomic numbering scheme (Fig. 1, S configuration) and with selected dimensions (Table 1). The geometric data are normal (McNab et al., 1997) and in agreement with expected values (Allen et al., 1987). The five- and six-membered rings of the isoindole group are essentially coplanar [dihedral angle between the rings = 0.6 (3)° (A) and 1.1 (2)° (B)] with the isoindolinone O3 atom displaced by 0.046 (4) Å (A) and 0.023 (4) Å (B) from the C4N ring planes; this ring is oriented at 64.80 (9)° (A) and 66.72 (9)° (B) to the phenol C6 ring. Molecules A and B are similar in conformation to the three independent molecules in the related L-tyrosine derivative (II) (Brady & Gallagher, 2000); minor differences are attributed to molecular deformation resulting from crystal packing (Table 1).

In (I), the acid molecules assemble as a dimeric unit in the asymmetric unit, but not via conventional [CO2H]2 R2(8) hydrogen-bonded rings, rather as an A/B acid pair with one
water molecule O1W forming an $R_3^{·}(10)$ ring (Fig. 1, Table 2). The other water O2W is positioned between O1W and the isoindole O3A, providing a complex arrangement of hydrogen-bonded rings with motifs $R_3^{·}(10)R_3^{·}(11) [R_2^{·}(15)]$ (Bernstein et al., 1995). Dimers link through (aryl A/B)O4—H4/C1/C1/C1/C1O3=C3B/aryl hydrogen bonds, forming a one-dimensional chain of rings connected as graph set $R_2^{·}(22)$ (Fig. 2), that associate further through centres of symmetry forming a column along [101], comprising two chains of rings linked and oriented in opposite directions. Such $R_2^{·}(22)$ rings are also a key feature in the crystal structure of (II). In (I), the column can also be described as assembling from dimers into tetramers (Fig. 3) and association into columns through (aryl)O—H/C1/C1/C1/O interactions (Fig. 4).

Columns interlock via π–π arene stacking interactions about inversion centres, forming ruffled sheets [isoindole C$_6$ ring interplanar distance of 3.37 Å, substantially offset with C$_{gl1}···C$_gl1$^vii = 3.769 (2) Å, where C$_{gl1}$ is the C4B–C9B ring centroid and symmetry code: (vii) $-x,-y,-z$], in tandem with C—H···π(arene) interactions (Fig. 5, Table 2) and C—H···O interactions. The cumulative effect yields a complex hydrogen-bond pattern as a three-dimensional network (Fig. 6).

The hydrogen bonding network involving O1W and O2W is uncommon as O2W forms only one strong hydrogen bond (Figs. 1–3). Water O1W is an acceptor for the acidic O1B—H1B group [O···O = 2.610 (3) Å, Table 2]. The O1B—H1 donor forms a bifurcated interaction with O3B$^{iii}$/O2A [O···O 2.982 (3)/3.149 (3) Å; symmetry operation $iii$, Table 2] and

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**Figure 1**
A view of molecules A, B, O1W and O2W in the asymmetric unit of (I), with the atomic numbering scheme; hydrogen bonds are drawn with dashed lines. Displacement ellipsoids are drawn at the 30% probability level.

**Figure 2**
A view of part of the one-dimensional chain of $R_2^{·}(22)$ rings in (I) with atoms drawn as small spheres of arbitrary radii and H atoms involved in hydrogen bonding included. Part of the phthalimidine rings have been omitted for clarity. Atom labels marked with # and $ are at the symmetry positions $(1 + x, y, 1 + z)$ and $(x - 1, y, z - 1)$, respectively.

**Figure 3**
A view of the hydrogen-bonded tetrameric unit in (I), with H atoms involved in interactions included and hydrogen bonds as dashed lines. Atoms marked with an asterisk * are at symmetry positions $(1 - x, -y, -z)$.
O1W—H2 with O2W [O···O 2.921 (4) Å] (Figs. 2, 3). The O2W water molecule is held loosely in the crystal structure, having larger displacement parameters than O1W. It accepts via O1W—H2···O2W but forms only one donor bond (via H3) with the nearest acceptor O3A [O···O = 3.133 (4) Å]. The other nearest potential acceptor is O1A at 3.508 (5) Å (contact distance). This does not arise on geometric grounds and H4 is located at appropriate electron density bonded to O2W but not oriented towards an acceptor atom/group.

Experimental

The title compound, (I), was prepared by the overnight reaction of β-L-leucine and o-phthalaldehyde in CH2CN under reflux conditions (Allin et al., 1996). Filtration of the hot solution and subsequent slow cooling of the filtrate allowed the isolation of block-like colourless crystals. Uptake of water as the acid–hydrate racemate presumably occurred during the crystallization process. M.p. 491–492 K (uncorrected). IR: (νC=O, cm⁻¹), 1737, 1640 (KBr).

Crystal data

C17H15NO4

M = 315.32

Monoclinic, P2₁/a

a = 15.5198 (10) Å

b = 14.7573 (12) Å

V = 3116.2 (5) Å³

Z = 4

Mo Kα radiation

µ = 0.10 mm⁻¹

T = 294 (1) K

Crystal data

V = 3116.2 (5) Å³

Z = 8

Mo Kα radiation

µ = 0.10 mm⁻¹

T = 294 (1) K

Data collection

Enraf–Nonius CAD-4

3983 measured reflections

Absorption correction: none

5769 independent reflections

Rint = 0.019

5983 measured reflections

Intensity decay: 1%

Refinement

R[F² > 2σ(F²)] = 0.049

H atoms treated by a mixture of independent and constrained refinement

wR² = 0.127

H atoms treated by a mixture of independent and constrained refinement

S = 0.96

H atoms treated by a mixture of independent and constrained refinement

R = 0.019

6 restraints

3 standard reflections

5769 reflections

Table 1

Selected torsion angles (°).

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<tr>
<th>Torsion angles</th>
<th>Values</th>
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<td>C3A—N1A—C2A—C2A</td>
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Figure 4

A view of the unit cell contents and the one-dimensional column in (I).

Figure 5

A stereoscopic view of the π···π stacking and C—H···π(arene) interactions for molecules B (about inversion centres, Table 2) with atoms depicted as their van der Waals spheres.

Table 2

Hydrogen-bond geometry (Å, °).

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<tr>
<th>D—H···A</th>
<th>D—H</th>
<th>D···A</th>
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<td>O1A—H1A···O2B</td>
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<td>0.93</td>
<td>2.85</td>
<td>3.723</td>
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</table>

Symmetry codes: (i) x,y,z; (ii) x + 1, y, z; (iii) x,y,z+1; (iv) –x + 1/2,y + 1/2,–z; (v) –x + 1/2,y + 1/2,–z; (vi) x,y,z+1; (vii) –x,y,z+1; (viii) –x,–y,–z.

Table 2

Hydrogen-bond geometry (Å, °).

H atoms attached to (C, O) in molecules A and B were treated as riding atoms, with C—H distances from 0.93 to 0.98 Å, O—H = 0.82 Å and with Uiso(H) from 1.2 to 1.5Ueq of the parent atom. For the
O1W and O2W water molecules, loose restraints were used for the O–H bond lengths at 0.91 (3)–0.93 (3) Å and with H···H distances restrained to 1.43 (3) Å; $U_{eq}(H) = 1.5U_{eq}(O)$.

Data collection: CAD4 (Enraf-Nonius, 1992); cell refinement: SET4 and CELDIM (Enraf-Nonius, 1992); data reduction: DATRD2 in NRCVAX96 (Gabe et al., 1989); program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); 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 and WORDPERFECT macro PREP8 (Ferguson, 1998).

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References