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

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(2*RS*)-3-(4-Hydroxyphenyl)-2-(1-oxo-1*H*-2,3-dihydro-isoindol-2-yl)propanoic acid monohydrate**John F. Gallagher* and Fiona Brady**

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Key indicators

Single-crystal X-ray study

 $T = 294$ KMean $\sigma(\text{C}-\text{C}) = 0.004$ Å R factor = 0.049 wR factor = 0.127

Data-to-parameter ratio = 13.4

For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

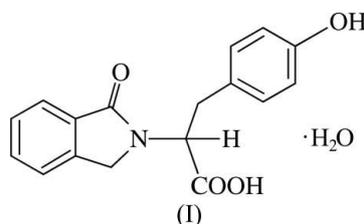
The title compound, $\text{C}_{17}\text{H}_{15}\text{NO}_4 \cdot \text{H}_2\text{O}$, derived from DL-tyrosine crystallizes as an unusual hydrogen-bonded acid–monohydrate dimer. The asymmetric unit contains two organic molecules and two water molecules. Dimers link through $(\text{aryl})\text{O}-\text{H} \cdots \text{O}=\text{C}$ hydrogen bonds along the [101] direction, forming a one-dimensional chain of rings, and further associated *via* inversion centres (forming a chain of rings aligned in the opposite direction) generating columns. Ruffled sheets arise from interlocking of isoindole rings *via* $\pi-\pi(\text{arene})$ stacking and $\text{C}-\text{H} \cdots \pi(\text{arene})$ interactions; $\text{C}-\text{H} \cdots \text{O}$ interactions generate a three-dimensional network.

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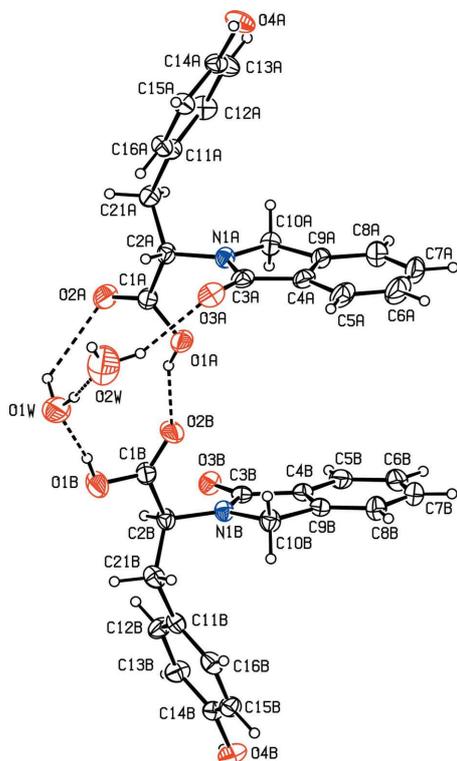
Comment

Structurally determined phthalimidine systems are mostly either *N*-substituted or have a hydroxy substituent at the 3-position (McNab *et al.*, 1997; Mukherjee *et al.*, 2000). The title compound, (I), synthesized from DL-tyrosine and *ortho*-phthalaldehyde (Allin *et al.*, 1996), forms part of a study of phthalimidines incorporating an aromatic residue (Brady *et al.*, 1998; Brady & Gallagher, 2000; Gallagher & Murphy, 1999).

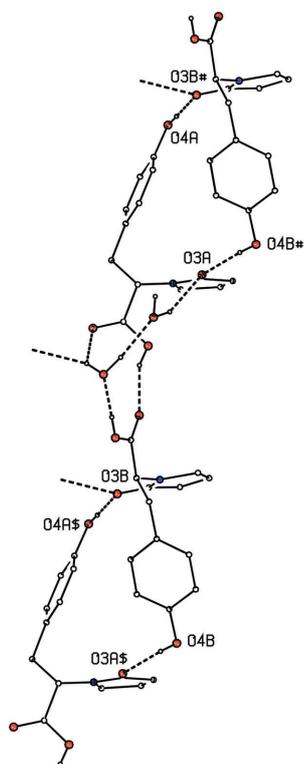


Compound (I) (derived from DL-tyrosine) crystallizes as a hydrogen-bonded acid–monohydrate dimer (with molecules *A/B*, *O1W*, *O2W* positioned to maximize hydrogen bonding within the asymmetric unit); this is depicted with the atomic numbering scheme (Fig. 1, *S* configuration) and with selected dimensions (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 C_4N ring planes; this ring is oriented at 64.80 (9°) (*A*) and 66.72 (9°) (*B*) to the phenol C_6 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).

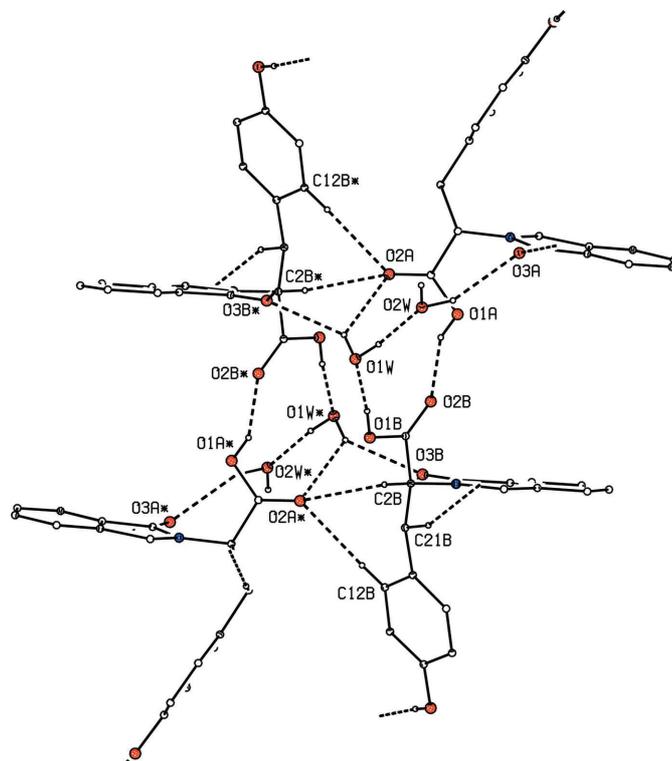
In (I), the acid molecules assemble as a dimeric unit in the asymmetric unit, but not *via* conventional $[\text{CO}_2\text{H}]_2$ $R_2^2(8)$ hydrogen-bonded rings, rather as an *A/B* acid pair with one

**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 $R_2^2(22)$ 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 $(1 - x, -y, -z)$.

water molecule O1W forming an $R_3^3(10)$ 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 $R_3^3(10)R_3^3(11)[R_4^4(15)]$ (Bernstein *et al.*, 1995). Dimers link through $(\text{aryl}_{A/B})\text{O}4-\text{H}4 \cdots \text{O}3=\text{C}3_{B/A}$ hydrogen bonds, forming a one-dimensional chain of rings connected as graph set $R_2^2(22)$ (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 $R_2^2(22)$ 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 $(\text{aryl})\text{O}-\text{H} \cdots \text{O}=\text{C}$ interactions (Fig. 4).

Columns interlock *via* $\pi-\pi$ arene stacking interactions about inversion centres, forming ruffled sheets [isoindole C₆ ring interplanar distance of 3.37 Å, substantially offset with $\text{Cg}1 \cdots \text{Cg}1^{\text{vii}} = 3.769(2)$ Å, where Cg1 is the C4B–C9B ring centroid and symmetry code: (vii) $-x, -y, -z$], in tandem with $\text{C}-\text{H} \cdots \pi(\text{arene})$ interactions (Fig. 5, Table 2) and $\text{C}-\text{H} \cdots \text{O}$ 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 [$\text{O} \cdots \text{O} = 2.610(3)$ Å, Table 2]. The O1W–H1 donor forms a bifurcated interaction with O3Bⁱⁱⁱ/O2A [$\text{O} \cdots \text{O} = 2.982(3)/3.149(3)$ Å; symmetry operation iii, Table 2] and

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 DL-leucine and *o*-phthalaldehyde in CH₃CN 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: ($\nu_{\text{C=O}}$ cm⁻¹), 1737, 1640 (KBr).

Crystal data

C ₁₇ H ₁₅ NO ₄ ·H ₂ O	$V = 3116.2 (5) \text{ \AA}^3$
$M_r = 315.32$	$Z = 8$
Monoclinic, $P2_1/a$	Mo $K\alpha$ radiation
$a = 15.5198 (10) \text{ \AA}$	$\mu = 0.10 \text{ mm}^{-1}$
$b = 14.7573 (12) \text{ \AA}$	$T = 294 (1) \text{ K}$
$c = 15.6383 (14) \text{ \AA}$	$0.35 \times 0.35 \times 0.27 \text{ mm}$
$\beta = 119.537 (7)^\circ$	

Data collection

Enraf–Nonius CAD-4 diffractometer	2889 reflections with $I > 2\sigma(I)$
Absorption correction: none	$R_{\text{int}} = 0.019$
5983 measured reflections	3 standard reflections
5769 independent reflections	frequency: 120 min
	intensity decay: 1%

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.049$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.127$	$\Delta\rho_{\text{max}} = 0.34 \text{ e \AA}^{-3}$
$S = 0.96$	$\Delta\rho_{\text{min}} = -0.22 \text{ e \AA}^{-3}$
5769 reflections	
432 parameters	
6 restraints	

Table 1

Selected torsion angles ($^\circ$).

C3A–N1A–C2A–C1A	–102.2 (3)	C3B–N1B–C2B–C1B	–107.9 (3)
C3A–N1A–C2A–C21A	131.0 (2)	C3B–N1B–C2B–C21B	125.4 (2)
O1A–C1A–C2A–N1A	18.8 (3)	O1B–C1B–C2B–N1B	–168.7 (2)
O1A–C1A–C2A–C21A	146.7 (2)	O1B–C1B–C2B–C21B	–42.1 (3)
C2A–N1A–C3A–O3A	–1.6 (4)	C2B–N1B–C3B–O3B	1.5 (4)

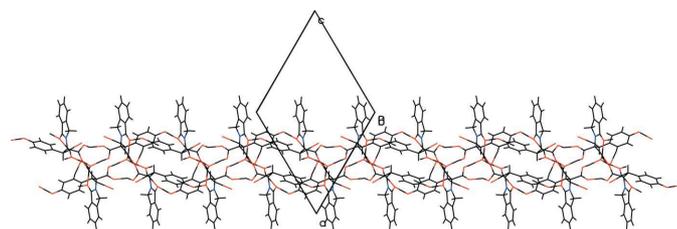


Figure 4
A view of the unit cell contents and the one-dimensional column in (I).

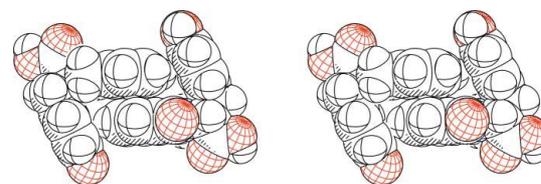


Figure 5

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.

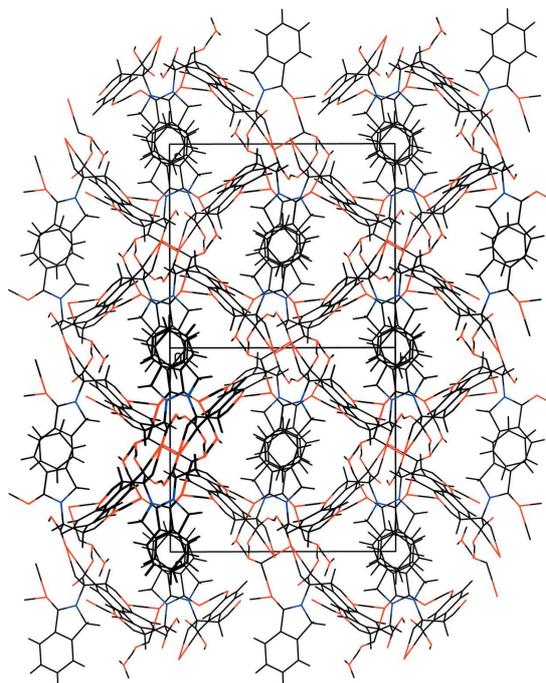


Figure 6

A packing diagram of (I) (view along the column).

Table 2

Hydrogen-bond geometry (Å, $^\circ$).

D–H···A	D–H	H···A	D···A	D–H···A
O1A–H1A···O2B	0.82	1.90	2.662 (3)	154
O1B–H1B···O1W	0.82	1.80	2.610 (3)	170
O1W–H1···O3B ⁱ	0.91 (3)	2.33 (3)	2.982 (3)	128 (3)
O1W–H1···O2A	0.91 (3)	2.48 (3)	3.149 (3)	130 (3)
O1W–H2···O2W	0.92 (2)	2.00 (2)	2.921 (4)	172 (4)
O2W–H3···O3A	0.93 (3)	2.27 (5)	3.133 (4)	154 (4)
O4A–H4A···O3B ⁱⁱ	0.82	1.85	2.670 (3)	178
O4B–H4B···O3A ⁱⁱⁱ	0.82	1.91	2.727 (3)	175
C2B–H2B···O2A ⁱ	0.98	2.52	3.438 (3)	157
C12B–H12B···O2A ⁱ	0.93	2.49	3.396 (3)	166
C21A–H21A···O4B ^{iv}	0.97	2.46	3.390 (3)	160
C21B–H21C···O4A ^v	0.97	2.54	3.448 (3)	156
C6A–H6A···Cg2 ^{vi}	0.93	2.83	3.707 (5)	158
C6B–H6B···Cg2 ^{vii}	0.93	2.85	3.723 (5)	157

Symmetry codes: (i) $-x+1, -y, -z$; (ii) $x+1, y, z+1$; (iii) $x-1, y, z-1$; (iv) $-x+\frac{1}{2}, y-\frac{1}{2}, -z$; (v) $-x+\frac{3}{2}, y+\frac{1}{2}, -z+1$; (vi) $x-\frac{1}{2}, -y-\frac{1}{2}, z+1$; (vii) $-x, -y, -z$.

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 $U_{\text{iso}}(\text{H})$ from 1.2 to 1.5 U_{eq} 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; $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{O})$.

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: NRCVAX96 and 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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