C—H···π_aren Csp³—H···O=C and O—H···O intermolecular interactions in (2R/2S)-3-(3-hydroxyphenyl)-2-(1-oxo-1,3-dihydro-2H-isooindol-2-yl)propanoic acid: a meta-tyrosine derivative

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(Received 22 July 1999; accepted 13 August 1999)

Abstract

The title compound, C₁₇H₁₅NO₄, a DL-meta-tyrosine derivative forms a hydrogen-bonded network in the solid state which consists of O_{acid}—H···O_{phenyl}—H···O=C_isooindole chains [O···O 2.668 (2) and 2.653 (2) Å], Csp³—H···O=C_{acid} [C···O 3.225 (3) Å] and two C—H···π_aren intermolecular interactions. The C—H···π_{phenyl} interaction is short, C···Cg 3.542 (3) Å, where Cg is the phenyl ring centroid (H···Cg 2.64 Å and C—H···Cg 165°). The interplanar angle between the five- and six-membered rings of the isooindole system is 0.95 (13)° with the carbonyl O atom 0.096 (3) Å from the C₄N ring plane. π—π stacking involving inversion symmetry-related isooindole groups occurs with RS pairs (interplanar distance of 3.43 Å).

Comment

Amino acid derivatives are a major class of chiral compounds with diverse applications in asymmetric synthesis and medicinal chemistry. DL-meta-Tyrosine (Byrkedal et al., 1974) and related compounds have attracted much interest, e.g. in biological studies (Kawai et al., 1999), not least due to the close structural relationship with L-dopa (Howard et al., 1995). The title compound, (I), a phthalimidine (isooindolin-1-one) derivative (Allin et al., 1996; McNab et al., 1997) is synthesized as a racemic mixture from DL-meta-tyrosine and forms part of a study of the hydrogen-bonding interactions and anion-recognition properties of a series of unnatural amino acid compounds (Dalton et al., 1999; Gallagher et al., 1999a,b).

The hydrogen bonding in (I) is dominated by O—H···O, C—H···O and C—H···π_{phenyl} interactions, detailed in Table 2 and depicted in Fig. 2. Conventional carboxylic acid O—H···O hydrogen bonding between pairs of carboxylic acid groups with graph set R_2^2(8) is not observed (Ferguson et al., 1995). Hydrogen bonding arises involving (i) the carboxylic acid O—H, phenolic O—H and phthalimidine carbonyl acceptor as O_{acid}—H···O_{phenyl}—H···O=C_isooindole systems with (ii)
Csp³−H⋯O=C acid and (iii) C−H⋯π arene interactions completing the intermolecular association. The crystal structure can be interpreted by considering RS pairs to associate through aromatic C−H⋯π interactions and π−π stacking about inversion centres. These RS dimers are linked through pairs of Ophenyl−H⋯O=Cisoindole hydrogen bonds forming a one-dimensional chain in the direction of the b axis (Fig. 2). The O−H⋯O−H⋯O=C systems link the one-dimensional chains with weaker Csp³−H⋯O=C acid and Csp³−H⋯π arene interactions forming a three-dimensional network.

Molecule (I) contains an extra O−H donor/acceptor in comparison to (II) which facilitates a shorter hydrogen bond along the O−H⋯O−H⋯O=C chain. In (II) the carboxylic acid O−H⋯O=Cisoindole hydrogen bond dominates in combination with C−H⋯O=C acid and two C−H⋯π interactions. The aromatic C6−H6⋯π interaction is present in both (I) and (II) with similar π−π stacking. The structure of (2S)-2-[(2R)-2-hydroxy-2-phenylethanoyl]amino]-4-methylpentanoic acid, (III), (Dalton et al., 1999) has a similar donor/acceptor set taking part in intermolecular interactions as (I) with two O−H⋯O=C hydrogen bonds, a Csp³−H⋯O=C acid and an aromatic C−H⋯π interaction present in (III). However, there are considerable structural and packing differences between (I) and (III).

The presence of C−H⋯O and C−H⋯π arene interactions with stronger hydrogen bonds e.g. O−H⋯O has been commented on previously (Steiner, 1997). The role of C−H⋯π arene interactions in controlling self-inclusion processes in calixarenes has been addressed (Ferguson et al., 1996). Theoretical calculations on the nature of C−H⋯π arene interactions have been reported in several organic systems with an estimation of the binding energy between the C−H donor and aromatic π cloud (Samanta et al., 1998), as well as with database studies (Malone et al., 1997). The role which these interactions play in protein structures has also been detailed (Umezawa & Nishio, 1998). However, a thorough understanding of the control and exploitation of X−H⋯π arene interactions (X = C, N, O) still remains an elusive goal in crystal-engineering studies (Braga et al., 1998). Further studies are in progress on related phthalimidine derivatives.

Experimental

The title compound was prepared by the overnight reaction of DL-m-tyrosine and o-phthalaldehyde in refluxing acetonitrile (Allin et al., 1996). Filtration of the hot solution and subsequent slow cooling of the filtrate allowed the isolation of large, colourless crystals. IR (νc~ν cm⁻¹): 1732, 1650 (KBr). Melting point 462-464 K (uncorrected). ¹H NMR data (400 MHz) (6, d6 DMSO, p.p.m.), 3.11 (m, 2H, CH₂), 4.41 (br s, 2H, CH₂), 5.07 (m, 1H, CH), 6.52-6.66, 6.98-7.02 (m, 4H, C₆H₄), 7.44-7.48, 7.56-7.65 (m, 4H, m-C₆H₄), 9.30 (s, 1H, O−H).

Crystal data

C₁₇H₁₅NO₄

M_r = 297.30

Monoclinic

P2₁/n

a = 11.3483 (15) Å

b = 8.9413 (10) Å

c = 14.705 (3) Å

β = 104.586 (13)°

V = 1444.0 (4) Å³

Z = 4

D_m not measured

D_x

not measured

Data collection

Enraf–Nonius CAD-4
diffractometer

ω–2θ scans

Absorption correction: none

2786 measured reflections

2684 independent reflections

1452 reflections with

I > 2σ(I)

Refinement

Refinement on F²

R[F² > 2σ(F²)] = 0.041

wR(F²) = 0.085

S = 0.941

2684 reflections

202 parameters

H atoms constrained

w = 1/[σ²(F²) + (0.0339P)²]

where P = (F² + 2F²)/3

(Δ/σ)max = 0.001

Δρ_max = 0.16 e Å⁻³

Δρ_min = −0.16 e Å⁻³

Extinction correction: SHEXL97 (Sheldrick, 1997a)

Extinction coefficient: 0.0111 (12)

Scattering factors from

International Tables for Crystallography (Vol. C)
Table 1. Selected geometric parameters (Å, °)

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<tr>
<th>Bond</th>
<th>Distance (Å)</th>
<th>Angle (°)</th>
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<td>1.196 (2)</td>
<td>N1–C10</td>
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<tr>
<td>O3–C3</td>
<td>1.236 (2)</td>
<td>C1–C2</td>
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<td>105.5 (2)</td>
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Table 2. Hydrogen-bonding geometry (Å, °)

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<tr>
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<td>162.7 (2)</td>
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<tr>
<td>C10–H10A–O2&quot;</td>
<td>2.32 (2)</td>
<td>139.5 (3)</td>
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<tr>
<td>C21–H21A–O2&quot;</td>
<td>2.36 (2)</td>
<td>129.0 (3)</td>
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</tbody>
</table>

Symmetry codes: (i) x-1/2, y, z; (ii) x, y, z; (iii) 1-x, 1-y, 1-z.

Molecule (I) as synthesized is a diastereomeric mixture and crystallized in the monoclinic space group P2_1/n determined from the systematic absences. H atoms were allowed for as riding atoms with C–H in the range 0.93–0.97 Å.


JFG thanks Dublin City University and Forbairt (International Collaboration grant IC/98/021) for funding a research visit to the University of Guelph (July–August, 1998) and especially Professor George Ferguson for use of his diffractometer and computer system.

Decabromodiphenyl ether

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(Received 19 November 1998; accepted 24 June 1999)

Abstract

Bis(pentabromophenyl) ether, C_{12}Br_{10}O, shows strange differences in the endocyclic angles between the two different rings, although they are both substituted in the same manner. Several short van der Waals contact...