Hydrogen bonds are formed with the heterocyclic C and C-O-H group O1 pair from an isoindolin-1-one system [compound interactions complete the hydrogen bonding, intermolecular interactions generate a cyclic motif through cooperativity, with shortest O...O and C...O distances of 2.634 (3) Å and 3.529 (5) Å, respectively. Methylene C-H...O=C indole interactions complete the hydrogen bonding, with C...O distances ranging from 3.283 (4) to 3.477 (4) Å.

Comment

Phthalimidines (isoindolin-1-ones) often display biological activity as potential anti-inflammatory agents and antipsychotics (Mukherjee et al., 2000), and most of the structurally determined systems are either N-substituted or have a hydroxy substituent at the 3-position (McNab et al., 1997; Kundu et al., 1999). Amino acids constitute a fundamental building block in biological compounds and valine derivatives have been utilized in the formation of chiral host lattices (Weigand et al., 1998). The title compounds, (2S)-2-(1-oxo-1H-2,3-dihydroisoindol-2-yl)pentanoic acid, (I), and (2S)-3-methyl-2-(1-oxo-1H-2,3-dihydroisoindol-2-yl)butanoic acid, (II), derived from l-norvaline and l-valine, respectively, form part of a systematic study of hydrogen-bonding interactions in a series of amino acid derivatives (Brady et al., 1998; Dalton et al., 1999; Gallagher & Murphy, 1999; Gallagher et al., 2000).

Compound (I) crystallizes in space group P212121 with one molecule in the asymmetric unit and a view of (I) with the atomic numbering scheme is given in Fig. 1, with selected dimensions in Table 1. The bond lengths and angles in the heterocyclic ring are similar to those reported previously (McNab et al., 1997; Brady et al., 1998; Gallagher & Murphy, 1999) and are in agreement with expected values (Orpen et al., 1994). The carboxylic acid group exhibits rotational disorder, with site occupancies of 0.55 (4) and 0.45 (4) for the major and minor orientations, respectively. The angle between the CO2 planes is 31 (3)° and the major CO2 orientation is at an angle of 67 (2)° to the C4N ring plane [87.1 (16)° for the minor site]. The angle between the five- and six-membered rings of the isoindole system is 1.37 (17)° and the maximum deviation from planarity for an atom in either ring plane is 0.0084 (16) Å for C9 (C4 ring), with the carbonyl O3 atom 0.026 (3) Å from the C4N ring plane. The n-propyl chain adopts two conformations, with site occupancies of 0.519 (11) and 0.481 (11); details are given in the Experimental section. The hydrogen bonding in (I) is dominated by O-H...O=C, C-H...O=C and C=C=C=H...O=C intermolecular interactions (Table 2 and Fig. 2). Conventional O-H...O hydrogen bonding is not observed, either between pairs of carboxylic acid groups [graph set R2(8); Ferguson et al., 1995] or through interaction of the COOH group with a C=H=C=O pair from an isoindolin-1-one system [compound (III); graph set R5(2); Brady et al., 1998]. Carboxylic acid O-H...O=C hydrogen bonds are formed with the heterocyclic ring C=O group O1A/O1B...O3 = 2.582 (13)/2.640 (12) Å [symmetry code: (i) 1 - x, y - 1/2, 1/2 - z, where B/A are the major/minor carboxylate sites. A C=C=C=H...O interaction involving the carboxylic acid C=O moiety as C7-C=H...O2A/B, with C=C=O = 3.231 (11)/3.49 (2) Å [symmetry code: (ii) 1/2 + x, 1/2 - y, 1 - z], generates a chain of C=C=C=H...O=C...O=O=C indole hydrogen bonds.

Figure 1
A view of (I) with the atomic numbering scheme. Atom labels with the suffix A indicate one of the disordered conformations of the carboxylic acid and n-propyl groups. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.
The orientation of the isoindole rings defined by C3–N1–C2–C1 is $95.3 (9)^\circ$, which is greater than the values of $-85.2 (2)^\circ$ in a related 3-phenylpropanoic acid derivative, (III) (Brady et al., 1998), or $-86.6 (2)^\circ$ in a meta-tyrosine derivative, (IV) (Gallagher & Murphy, 1999), but smaller than the values of $-104.5 (3)^\circ$ and $-112.29 (14)^\circ$ in the chiral, (V), and racemic forms, (VI), of related threonine structures (Gallagher et al., 2000).

Compound (II) crystallizes in space group $P1$, with two independent molecules, $A$ and $B$, in the asymmetric unit, which differ slightly in conformation but retain the same configuration ($S$) at the chiral centre. A view of the asymmetric unit with the atomic numbering scheme is given in Fig. 3 and selected dimensions are given in Table 3. Bond lengths and angles are in accord with anticipated values (Orpen et al., 1994). The r.m.s. deviation for the superposition of the non-H atoms in both molecules is 0.39 Å (Spek, 1998). The angles between the five- and six-membered rings of the isoindole system are 1.0 (2) ($A$) and 1.7 (2) ($B$), and the maximum deviation from planarity for an atom in either indole ring is 0.010 (3) Å for $C7A$, with the carbonyl $O3$ atom 0.039 (5) ($A$) and 0.036 (5) ($B$) from the $C9N$ ring plane. The angles between the $CCO_2$ group and the $C9N$ ring planes are $77.51 (11)$ and $79.28 (11)^\circ$ in molecules $A$ and $B$, respectively. Torsion angle differences are evident from $N1$–$C1$–$C12$ with values of $-43.6 (4)$ ($A$) and $-52.0 (3)^\circ$ ($B$) (Table 3).

The orientations of the isoindole rings defined by C3–N1–C2–C1 are $57.3 (4)$ ($A$) and $60.7 (4)^\circ$ ($B$), and these values are opposite to those in structures (I)–(VI), presumably due to steric hindrance of the isopropyl group in (II) compared with the $n$-propyl group in (I).

The hydrogen bonding in (II) is dominated by O–H···O=C, C–H···O=C and $Csp^2$–H···O intermolecular interactions (Table 4 and Fig. 4). Hydrogen-bonded rings with graph set $R_2^2(9)$ are formed from the combination of acid $O1_{A/B}$–$H1$···$O3_{B/A}$ interactions with the heterocyclic ring $C=C$ group $[2.642 (3)$ and $2.634 (3)$ Å, respectively] and arene $C8_{B/A}$–$H5$···$O2_{A/B}$ contacts with the carboxylic acid $C=C$ group $[3.529 (5)$ and $3.714 (5)$ Å, respectively]. The $R_2^2(9)$ motif is present in a related 3-phenylpropanoic acid system, (III) (Brady et al., 1998). This cooperativity generates a hydrogen-bonded zigzag chain in the direction of the $a$ and $b$ axes. The hydrogen-bonded network is completed by $C10$–$H10$···$O3$ interactions in which all four, of the four $H$ atoms, $H10A$ and $H10B$ in $A$, and $H10C$ and $H10D$ in $B$, participate. The $C5$–$H5$···$O2$ distances are longer in (II) than those in (III), although the O···O distances are similar. This $C$···$O$ difference may be due to the weak intramolecular $C13$–$H13$···$O2$ contacts present in both molecules of (II).

The hydrogen bonding in (I) and (II) is similar in terms of hydrogen-bond numbers and associated distances per molecule, with one O–H···O, two C–H···O and a C–H···$\pi_{\text{arom}}$ interaction in (I), comparable with the O–H···O and three C–H···O interactions per molecule in (II). The unit-cell volumes of $1265.3 \, \text{Å}^3$ in (I) and $584.6 \, \text{Å}^3$ in (II) show a difference of $24 \, \text{Å}^3$ per molecule $[316 \, \text{Å}^3$ in (I) and $292 \, \text{Å}^3$ in (II)], which can be accounted for by the carboxylic acid and $n$-propyl-group disorder in (I). The rotational disorder of the carboxylic acid group is assisted by the looser interactions involving the carboxylate $O2$ atom in (I). Examination of (II) and the major conformation of (I) with $PLATON$ (Spek, 2000),

Figure 2
A view of the intermolecular interactions of (I) with the major conformation only; symmetry codes are as given in Table 2.
1998) showed that there were no solvent-accessible voids in either crystal lattice. The hydrogen bonding in (II) can be compared with that of the two independent molecules which differ slightly in conformation in N,N’dicyclohexyl-N-(3-pyridylcarbonyl)urea (Gallagher et al., 1999). The overall crystal structure of (II) may be facilitated through hydrogen-bonded oligomeric units crystallizing from solution to produce the primary [A····B···]n hydrogen-bonded chain.

Figure 4
A view of the intermolecular interactions in (II); symmetry codes are as given in Table 4.

Experimental
The title compounds, (I) and (II), were prepared by the overnight reaction of o-phenaldehyde with l-norvaline and l-valine, respectively, in refluxing CH3CN under N2 (Allin et al., 1996). Filtration of the hot solution and subsequent slow cooling of the filtrate allowed the isolation of large colourless crystals from CH3CN. Spectroscopic analysis for (I), m.p. 467–468 K (uncorrected): IR (κbr cm−1): 1730, 1649 (KBr); 1H NMR (400 MHz, δ, d6-DMSO): 0.89 (t, 3H, CH3), 1.29 (br m, 2H, CH2), 1.90 (br m, 2H, CH2), 4.49 (q, 2H, CH2), 4.77 (m, 1H, CH), 7.48–7.51, 7.69–7.72 (m, 4H, C6H4). Spectroscopic analysis for (II), m.p. 436–438 K (uncorrected): IR (κbr cm−1): 1734, 1647, 1634 (KBr); 1H NMR (400 MHz, δ, d6-DMSO): 0.84 (d, 3H, CH3), 1.02 (d, 3H, CH3), 2.29 (br m, 1H, CH), 4.53 (m, 2H, CH2), 4.63 (m, 1H, CH), 7.30–7.37, 7.69–7.72 (m, 4H, C6H4).

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

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<tr>
<th></th>
<th>O3—C3</th>
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<th>C2—C11</th>
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<td>N1—C3</td>
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<td>C3—C4</td>
<td>1.467 (3)</td>
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<tr>
<td>N1—C2</td>
<td>1.444 (3)</td>
<td>C9—C10</td>
<td>1.490 (3)</td>
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<tr>
<td>N1—C10</td>
<td>1.461 (3)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>C2—N1—C3</td>
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<td>N1—C3—C4</td>
<td>107.5 (2)</td>
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<tr>
<td>C2—N1—C10</td>
<td>124.3 (2)</td>
<td>C3—C4—C5</td>
<td>130.5 (2)</td>
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</tr>
<tr>
<td>C3—N1—C10</td>
<td>112.6 (2)</td>
<td>C4—C9—C10</td>
<td>108.0 (2)</td>
<td></td>
</tr>
<tr>
<td>N1—C2—C11</td>
<td>112.9 (2)</td>
<td>C4—C9—C10</td>
<td>108.5 (2)</td>
<td></td>
</tr>
<tr>
<td>C3—C3—N1</td>
<td>123.9 (2)</td>
<td>C8—C9—C10</td>
<td>129.9 (2)</td>
<td></td>
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<tr>
<td>C3—C3—C4</td>
<td>128.5 (2)</td>
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<tr>
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<td>−95.3 (9)</td>
<td>C3—N1—C2—C1B</td>
<td>−95.8 (11)</td>
<td></td>
</tr>
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Table 2
Hydrogen-bonding geometry (Å, °) for (I).

<table>
<thead>
<tr>
<th></th>
<th>D—H···A</th>
<th>D—H</th>
<th>H···A</th>
<th>D—A</th>
<th>D—H···A</th>
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<tbody>
<tr>
<td>O1A—H1A···O3</td>
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<td>1.54</td>
<td>2.582 (13)</td>
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<tr>
<td>O1B—H1B···O3</td>
<td>0.98</td>
<td>1.74</td>
<td>2.640 (12)</td>
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<tr>
<td>C7—H7···O2A</td>
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<td>2.66</td>
<td>3.49 (2)</td>
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<td>149</td>
</tr>
<tr>
<td>C8—H8···C10</td>
<td>0.93</td>
<td>2.74</td>
<td>3.466 (3)</td>
<td>136</td>
<td>136</td>
</tr>
<tr>
<td>C10···H10A···O3</td>
<td>0.97</td>
<td>2.49</td>
<td>3.335 (3)</td>
<td>146</td>
<td>146</td>
</tr>
</tbody>
</table>

Symmetry codes: (i) 1−x, y, 1−z; (ii) 1+x, −y, z; (iii) 1−x, y, z.

Compound (II)

Crystal data
C13H15NO3
Mr = 233.26
Triclinic, P1
a = 5.8767 (6) Å
b = 9.9036 (13) Å
c = 10.4818 (15) Å
α = 103.327 (13)°
β = 109.759 (11)°
γ = 89.792 (11)°
Z = 2
V = 584.62 (13) Å3

Gallagher and Brady • Two isomers of C13H15NO3

621
organic compounds

Data collection

Enraf–Nonius CAD-4 diffractometer
ω/2θ scans
5259 measured reflections
2575 independent reflections
2059 reflections with I > 2σ(I)
R_{	ext{int}} = 0.014

θ_{\text{max}} = 27°

h = -7 to 7

k = -12 to 12

l = -13 to 13

Table 4

<table>
<thead>
<tr>
<th>D–H · · · A</th>
<th>D–H · · · A</th>
<th>D–H · · · A</th>
<th>D–H · · · A</th>
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</thead>
<tbody>
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<td>CO–H · · · N1</td>
<td>0.82</td>
<td>1.93</td>
<td>2.642 (3)</td>
</tr>
<tr>
<td>CS–H · · · O21</td>
<td>0.93</td>
<td>2.68</td>
<td>3.529 (5)</td>
</tr>
<tr>
<td>C10–H10B · · · O31</td>
<td>0.97</td>
<td>2.43</td>
<td>3.314 (4)</td>
</tr>
<tr>
<td>C10–H10A · · · O31</td>
<td>0.97</td>
<td>2.58</td>
<td>3.477 (4)</td>
</tr>
<tr>
<td>O1B–H1B · · · O31</td>
<td>0.82</td>
<td>1.87</td>
<td>2.634 (3)</td>
</tr>
<tr>
<td>C3B–H3B · · · O21</td>
<td>0.93</td>
<td>2.86</td>
<td>3.714 (5)</td>
</tr>
<tr>
<td>C10B–H10C · · · O1A</td>
<td>0.97</td>
<td>2.56</td>
<td>3.455 (4)</td>
</tr>
<tr>
<td>C10B–H10D · · · O31</td>
<td>0.97</td>
<td>2.46</td>
<td>3.283 (4)</td>
</tr>
</tbody>
</table>

Symmetry codes: (i) x, 1 + y, z; (ii) x − 1, y, z; (iii) x − 1, 1 + y, z; (iv) x, y − 1, z; (v) 1 − x, y, z

For both compounds, all atoms bound to C were treated as riding, with the SHELXL97 (Sheldrick, 1997) defaults for C–H distances and with U_{eq}(H) = 1.5U_{eq}(C) for methyl H atoms and 1.2U_{eq}(C) for the remainder. For (I), the H-atom sites of O–H were located from difference Fourier maps in the penultimate stages of refinement and were included at these positions in the calculations, with O–H distances of 1.07 and 0.98 Å, while for (II), the H atom bound to O was located from a difference Fourier map and subsequently treated as a rigid rotating group, with U_{eq}(H) = 1.5U_{eq}(O). The absolute structures of (I) and (II) were not reliably determined by our X-ray analysis, but they can be inferred from the known absolute configurations of the L-valine and L-valine in the synthesis of (I) and (II), respectively.

For both compounds, data collection: CAD-4-PC Software (Enraf–Nonius, 1992); cell refinement: CAD-4-PC Software; data reduction: NRCVAX96 (Gabe et al., 1989); program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: NRCVAX96 and SHELXL97; molecular graphics: ORTEPIII (Burnett & Johnson, 1996), ORTEP (McArdle, 1995) and PLATON (Spek, 1998); software used to prepare material for publication: NRCVAX96, SHELXL97 and PREP8 (Ferguson, 1998).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1085). Additional figures are also available. Services for accessing these data are described at the back of the journal.

References


