Refinement on $F^2$

$R[F^2 > 2\sigma(F^2)] = 0.025$

$wR(F^2) = 0.058$

$S = 1.079$

1818 reflections

177 parameters

H atoms: see below

$\Delta\sigma_{\text{max}} = 0.009$

$\Delta\rho_{\text{max}} = 1.155$ eÅ$^{-3}$

$\Delta\rho_{\text{min}} = -0.875$ eÅ$^{-3}$

Extinction correction:

$\text{SHELXL97}$

Extinction coefficient:

$w = 1/\sigma^2(F^2) + (0.017P)^2$ + 2.630P

where $P = (F^2 + 2F^2)/3$

Scattering factors from International Tables for Crystallography (Vol. C)

Table 1. Hydrogen-bonding geometry (Å, °)

<table>
<thead>
<tr>
<th>D—H⋯A</th>
<th>D—H</th>
<th>H⋯A</th>
<th>D⋯A</th>
<th>D—H⋯A</th>
</tr>
</thead>
<tbody>
<tr>
<td>O1—H1⋯N1</td>
<td>1.84 (12)</td>
<td>2.73 (5)</td>
<td>171 (4)</td>
<td></td>
</tr>
<tr>
<td>O2—H2⋯N2</td>
<td>1.89 (15)</td>
<td>2.76 (4)</td>
<td>164 (4)</td>
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<tr>
<td>O3—H3⋯O2</td>
<td>2.12 (3)</td>
<td>2.86 (3)</td>
<td>140 (4)</td>
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<tr>
<td>N1—H12⋯I</td>
<td>3.01 (2)</td>
<td>3.78 (3)</td>
<td>145 (3)</td>
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</tr>
<tr>
<td>N3—H32⋯I</td>
<td>2.91 (3)</td>
<td>3.78 (3)</td>
<td>167 (3)</td>
<td></td>
</tr>
<tr>
<td>N3—H33⋯O</td>
<td>2.91 (2)</td>
<td>3.79 (3)</td>
<td>167 (3)</td>
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<tr>
<td>N2—H22⋯I</td>
<td>2.96 (3)</td>
<td>3.79 (3)</td>
<td>167 (3)</td>
<td></td>
</tr>
</tbody>
</table>

Symmetry codes: (i) 1 -x, 1 -y, -z; (ii) 1 -x, 1 -y, 1 -z; (iii) x, y, z- 1; (iv) ½+x, 3-y, z- ½; (v) ¾-x, ½+y, ½-z.

400 exposures were taken in the 0–360° ϕ range with a crystal-to-detector distance of 60 mm and an exposure time of 1 min. Constant-circle profiles (17 pixels) without allowing overlap were used for integration, yielding a 92.8% completeness of data. A numerical absorption correction (Stoe & Cie, 1996) was applied using optically determined crystal faces (Stoe & Cie, 1997). The refined maximum and minimum electron densities of 1.155 and -0.875 eÅ$^{-3}$ were located only 0.79 and 0.72 Å from the iodide counter-ion, allowing overlap were used for integration, yielding a 92.8% completeness of data. A numerical absorption correction (Stoe & Cie, 1996) was applied using optically determined crystal faces (Stoe & Cie, 1997). The refined maximum and minimum electron densities of 1.155 and -0.875 eÅ$^{-3}$ were located only 0.79 and 0.72 Å from the iodide counter-ion, respectively. The atomic coordinates of all H atoms were found from difference Fourier syntheses. The atomic coordinates and individual $U_{iso}$ values were refined for the two NH$_2$, the NH$_3$ and the OH group with the X—H distances restrained to plausible values. The atomic coordinates of H atoms bonded to C atoms were refined with the C—H distance restrained to a plausible value and the $U_{iso}$ value set to 1.2$U_{eq}$(C).


Supplementary data for this paper are available from the IUCr electronic archives (Reference: IZ1311). Services for accessing these data are described at the back of the journal.

References


Stoe & Cie, Darmstadt, Germany.


JOHN P. DALTON,* JOHN F. GALLAGHER,* PETER T. M. KENNY, and MICHAEL O’DONOHUE

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Abstract

The title compound, C$_{14}$H$_{19}$NO$_4$+$^+$I$^-$, forms a hydrogen-bonded network in the solid state, consisting of one intramolecular N—H⋯O [N⋯O 2.569 (3) Å] and two intermolecular O—H⋯O=C [O⋯O 2.704 (2) and...
2.801 (2) Å hydrogen bonds, with weaker C—H···O [C···O 3.344 (3) Å] and Csp$^3$—H···πinteraction [shortest C···C 3.873 (4) Å] interactions completing the three-dimensional network.

**Comment**

The study of biologically active molecules is of primary importance in medicinal chemistry. Processes such as hormone synthesis, viral replication and cancer cell invasion are critically dependent on protease enzymes, which have become attractive target molecules in drug design. Many inhibitors are based on modified amino acids which incorporate the basic structural features determining normal enzyme–substrate interactions. The general principles underlying molecular recognition processes are reasonably well understood and hydrogen bonding in crystal structures can often be rationalized in preferred combinations of hydrogen-bond donors and acceptors (Etter *et al.*, 1990). In molecules where several different potential hydrogen-bond donors and acceptors are present (with cooperativity among these interactions), the ability to deduce in advance the molecular packing arrangements in the crystal structure remains a largely unrealised vision (Wolff, 1996). The title compound, (I), is part of a study of hydrogen-bonding interactions in amino acid derivatives and is of relevance in the design of antimalarial drugs.

A view of molecule (I) (RS configuration) with our numbering scheme is given in Fig. 1 and selected dimensions are in Table 1. The bond lengths and angles are in agreement with expected values (Orpen *et al.*, 1994). The phenyl ring is almost perpendicular to both the C2/N1/C3/O3/C4/O4 plane [86.60 (6)°] and the carboxylic acid O1/O2/C1/C2 group [76.45 (9)°]; C2/N1/C3/O3/C4/O4 is at an angle of 52.83 (7)° to the O1/O2/C1/C2 plane. Examination of the structure with PLATON (Spek, 1997a) indicated that there were no solvent-accessible voids in the crystal lattice.

Extensive hydrogen bonding is present in the crystal structure, consisting of an intramolecular N—H···O and two intermolecular O—H···C hydrogen bonds, as well as C—H···O and Csp$^3$—H···πinteraction interactions, such that all potential hydrogen-bond donors and acceptors engage in hydrogen bonding. A view is given in Fig. 2, with details in Table 2. The intramolecular N1—H11···O4 hydrogen bond [graph set S(5)] is listed with the N1···O2 dimensions for comparison. The distinction between weak hydrogen bonds and van der Waals interactions has been commented on by Steiner & Desiraju (1998).
Conventional intermolecular carboxylic acid O—H···O hydrogen bonding between pairs of carboxylic acid groups with graph set R₂(8) is not observed (Ferguson et al., 1995). Hydrogen-bonded rings with graph set R₂(9) are formed from the combination of (a) carboxylic acid O1—H1···O3¹ interactions with the amide C=C=O group, where O1···O3¹ is 2.704 (2) Å [symmetry code: (i) 1 − x, y − ½, −z] and (b) C2—H2···O3ii interactions with the carboxylic acid C=O moiety, where C···O³ii is 3.344 (3) Å [symmetry code: (iii) 1 − x, y + ½, −z]. This R₂(9) motif is also present in (2R/2S)-2-(1-oxo-1,3-dihydro-2H-isoindol-2-yl)-3-phenylpropanoic acid, with O···O and C···O distances of 2.625 (2) and 3.281 (3) Å, respectively (Brady et al., 1998). The O4—H41 alcohol group takes part in hydrogen bonding with the amide O3, and C2—H2···O4vi interactions with the carboxylic acid C=O moiety, where C···O4vi is 3.344 (3) Å [symmetry code: (iv) 1 − x, y, −z].

Weak Csp³—H···π interactions, for instance C8···Cgliv [3.939 (3) Å; CglI is the ring centroid of the arene ring; symmetry code: (iv) 1 + x, y, z], complete the intermolecular interactions. C—H···π interactions have been previously shown to have a profound effect on the molecular packing patterns of macrocycles (Ferguson et al., 1996). Further studies are in progress on related amino acid derivatives.

**Experimental**

Synthesis of the title compound was carried out as follows: NaOH (25 ml, 1 M) was added to a solution of N-[[(R/S)-2-acetoxy-2-phenylacetly]-l-leucine methyl ester (3.2 g, 0.01 mol) in CH₂O (20 ml) and stirred at room temperature for 1 h. The solution was cooled to 273 K and acidified with 10% HCl; the CH₃OH was removed in vacuo. A crystal with the diastereomers in the solid state. A crystal with the following data (100 MHz, 6, DMSO, p.p.m.): 173.79, 171.94 (−CO, H aromatic), 7.98-8.00 (2H, d, J = 8.88 Hz, NH); 31C NMR data (400 MHz, δ, DMSO, p.p.m.): 7.95–0.85 [12H, m, C(CH₃)₂], 1.46–1.66 (6H, m, CH₂CH), 4.22–4.28 (2H, m, NCHCO₂), 1.46–1.66 (6H, m, CH₂CH), 4.22–4.28 (2H, m, NCHCO₂), 1.46–1.66 (6H, m, CH₂CH), 4.22–4.28 (2H, m, NCHCO₂), 1.46–1.66 (6H, m, CH₂CH), 4.22–4.28 (2H, m, NCHCO₂).

**Table 1. Selected geometric parameters (Å, °)**

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<tr>
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<td>1.23</td>
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</tr>
</tbody>
</table>

**Table 2. Hydrogen-bonding geometry (Å, °)**

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</table>

Molecule (I), which is chiral, crystallized as RS and SS diastereomers in the solid state. A crystal with the RS configuration at the two chiral centres was chosen for examination; space group P₂₁ was concluded from the systematic absences. A full 'Friedel' data set was collected for this structure.
although the anomalous dispersion terms for O, N and C are small. The absolute structure was not determined [Flack parameter −0.9 (12)] by our X-ray analysis, but can be inferred from the known absolute configuration of the L-leucine methyl ester derivative used in the synthesis. The H atoms attached to O and N were located from difference maps at an intermediate stage of refinement and were refined with isotropic displacement parameters. The N—H and two O—H distances refined to 0.84 (3), 0.88 (4) and 0.87 (3) Å, respectively. The H atoms attached to C were treated as riding atoms, with the C—H bond lengths in the range 0.93 to 0.98 Å.

Data collection: CAD-4-PC Software (Enraf–Nonius, 1992), Cell refinement: SHELX97 and CELDIM in CAD-4-PC Software. Data reduction: DATRDR2 in NRCVAX96 (Gabe et al., 1989). Program(s) used to solve structure: SHELXS97 (Sheldrick, 1997b). Program(s) used to refine structure: NRCVAX96 and SHELXL97 (Sheldrick, 1997a). Molecular graphics: NRCVAX96, ORTEPII (Johnson, 1976), PLATON (Spek, 1997a) and PLUTON (Spek, 1997b). Software used to prepare material for publication: NRCVAX96, SHELXL97 and PRPCIF97 (Ferguson, 1997).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1269). Services for accessing these data are described at the back of the journal.

References