Refinement

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
$w = 1/[\sigma^2(F_o^2) + (0.017P)^2 + 2.630P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.009$
$\Delta\rho_{max} = 1.155$ e Å^{-3}
$\Delta\rho_{min} = -0.875$ e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0041 (6)
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···N1^{i}	0.895 (10)	1.843 (12)	2.730 (3)	171 (4)
O2—H2···N2^{ii}	0.892 (10)	1.897 (15)	2.765 (4)	164 (4)
O3—H3···O2	0.890 (10)	2.12 (3)	2.865 (3)	140 (4)
N1—H12···I^{ii}	0.894 (10)	3.01 (2)	3.782 (3)	145 (3)
N3—H31···I^{iii}	0.892 (10)	2.914 (13)	3.788 (3)	167 (3)
N3—H32···I^{iv}	0.896 (10)	2.944 (15)	3.807 (3)	162 (3)
N3—H33···O^{v}	0.896 (10)	2.019 (12)	2.908 (3)	171 (4)
N2—H22···I	0.894 (10)	2.96 (3)	3.729 (3)	145 (4)

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

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 difference electron densities of 1.155 and −0.875 e Å^3 were located only 0.79 and 0.72 Å from the iodide counter-ion, respectively. The atomic coordinates of all H atoms were taken 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 $1.2U_{eq}$(C).

Data collection: *IPDS Software* (Stoe & Cie, 1997). Cell refinement: *IPDS Software*. Data reduction: *IPDS Software*. Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*b*). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997*a*). Molecular graphics: *SHELXTL-Plus* (Sheldrick, 1992). Software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1311). Services for accessing these data are described at the back of the journal.

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Intramolecular N—H···O, intermolecular O—H···O, C—H···O and Csp^3—H···π_{arene} interactions in (2*S*)-2-{[(2*R*)-2-hydroxy-2-phenylethanoyl]amino}-4-methylpentanoic acid

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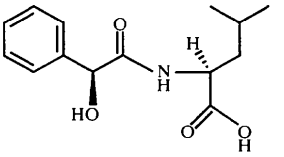
Abstract

The title compound, $C_{14}H_{19}NO_4$, 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···π_{arene} [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.



(I)

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, 1997*a*) 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···O=C hydrogen bonds, as well as C—H···O and Csp^3—H···π_{arene} 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).

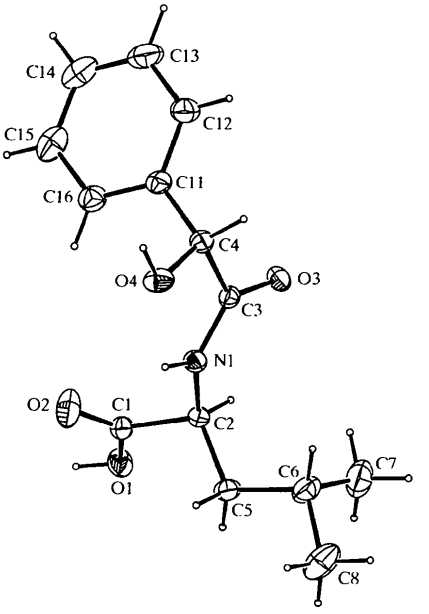


Fig. 1. A view of (I) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

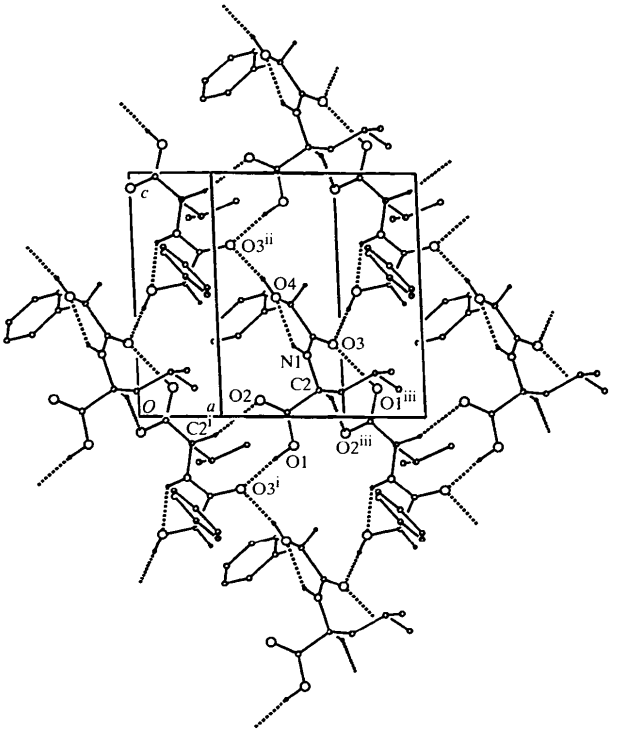


Fig. 2. A view of the unit cell and the hydrogen-bonding interactions. Symmetry codes are as given in Table 2.

Conventional intermolecular 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-bonded rings with graph set $R_2^2(9)$ are formed from the combination of (*a*) carboxylic acid O1—H1···O3^{i} interactions with the amide C=O group, where O1···O3^{i} is 2.704 (2) Å [symmetry code: (i) $1 - x, y - \frac{1}{2}, -z$] and (*b*) C2—H2···O2^{iii} interactions with the carboxylic acid C=O moiety, where C···O^{iii} is 3.344 (3) Å [symmetry code: (iii) $1 - x, \frac{1}{2} + y, -z$]. This $R_2^2(9)$ motif is also present in (2*R*/2*S*)-2-(1-oxo-1,3-dihydro-2*H*-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 O4···O3^{ii} = 2.801 (2) Å [symmetry code: (ii) $1 - x, y - \frac{1}{2}, 1 - z$]; H11···O4—H41 is 163.8 (19)° and the H1^{iii}···O3···H41^{v} angle is 90.7 (15)° [symmetry code: (v) $1 - x, \frac{1}{2} + y, 1 - z$].

Weak C*sp*^{3}—H···π_{arene} interactions, for instance C8···*Cg*1^{iv} [3.939 (3) Å; *Cg*1 is the ring centroid of the phenyl ring; symmetry code: (iv) $1 + x, y, z$], complete the intermolecular interactions. C—H···π_{arene} 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-phenylacetyl]-L-leucine methyl ester (3.2 g, 0.01 mol) in CH_3OH (20 ml) and stirred at room temperature for 1 h. The solution was cooled to 273 K and acidified with 10% HCl; the CH_3OH was removed *in vacuo*. Recrystallization of the resulting precipitate from acetone/*n*-hexane yielded crystals suitable for X-ray analysis [yield 2.3 g, 87%; m.p. 389–391 K (uncorrected)]. ^{1}H NMR data (400 MHz, δ, DMSO, p.p.m.): 0.75–0.85 [12H, *m*, C(CH_3)$_2$], 1.46–1.66 (6H, *m*, CH_2CH), 4.22–4.28 (2H, *m*, $NCHCO_2$), 4.93 (2H, *s*, OH), 6.25 (2H, *s*, PhCH), 7.22–7.40 (10H, *m*, ArH), 7.98–8.00 (2H, *d*, *J* = 8.88 Hz, NH); ^{13}C NMR data (100 MHz, δ, DMSO, p.p.m.): 173.79, 171.94 (–CO_2H and –C=O), 141.25, 127.89, 127.38, 126.62 ($C_{aromatic}$), 73.28 (–CHOH), 49.75 (–NHCH), 24.32 (–CH_2), 22.83, 21.36 [$CH(CH_3)_2$] (note: the signals at 173.79 and 171.94 may be interchangeable); MS, *M*–H_2O found: 247.1322, $C_{14}H_{17}NO_3$ requires 247.1207; *m*/*z* (%): 247 (0.5) (*M*–H_2O), 107 (100), 86 (22), 77 (19); infrared spectroscopy, ν_{max}(KBr), cm^{-1}: 3459 (OH), 3389 (NH), 3296, 1725 (carboxylic acid C=O), 1639 (amide C=O), 1556, 1267, 1160.

Crystal data

$C_{14}H_{19}NO_4$
M_r = 265.30
Monoclinic
$P2_1$
a = 8.5887 (10) Å
b = 8.6404 (6) Å
c = 9.6169 (6) Å
β = 98.398 (7)°
V = 706.02 (11) Å^3
Z = 2
D_x = 1.248 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.7107 Å
Cell parameters from 25 reflections
θ = 10.40–19.65°
μ = 0.091 mm^{-1}
T = 294 (1) K
Plate
0.38 × 0.32 × 0.14 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
3225 measured reflections
3133 independent reflections
2540 reflections with $I > 2\sigma(I)$
R_{int} = 0.008
θ_{max} = 27.4°
$h = -11 \rightarrow 11$
$k = -11 \rightarrow 11$
$l = 0 \rightarrow 12$
3 standard reflections
frequency: 120 min
intensity variation: 1.0%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.119
S = 1.013
3133 reflections
185 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.0786P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.164 e Å^{-3}
$\Delta\rho_{min}$ = −0.151 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997*a*)
Extinction coefficient: 0.037 (8)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = −0.9 (12)

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

O1—C1	1.314 (2)	O4—C4	1.423 (2)
O2—C1	1.200 (3)	N1—C2	1.451 (2)
O3—C3	1.239 (2)	N1—C3	1.322 (2)
C2—N1—C3	126.97 (18)	O3—C3—N1	124.95 (17)
O1—C1—O2	124.81 (19)	O3—C3—C4	119.48 (16)
O1—C1—C2	112.69 (17)	N1—C3—C4	115.49 (17)
O2—C1—C2	122.44 (18)	O4—C4—C3	108.22 (15)
N1—C2—C1	107.21 (15)	O4—C4—C11	112.68 (16)
N1—C2—C5	111.94 (16)		
O2—C1—C2—N1	−18.1 (3)	O3—C3—C4—O4	−166.85 (16)
C2—N1—C3—O3	−11.0 (3)	N1—C3—C4—O4	16.1 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H11···O4	0.84 (3)	2.09 (2)	2.569 (3)	116 (2)
N1—H11···O2	0.84 (3)	2.49 (2)	2.650 (3)	92 (2)
O1—H1···O3^{i}	0.88 (4)	1.83 (4)	2.704 (2)	170 (3)
O4—H41···O3^{ii}	0.87 (3)	1.95 (3)	2.801 (2)	168 (3)
C2—H2···O2^{iii}	0.98	2.41	3.344 (3)	159
C8—H8*A*···*Cg*1^{iv}	0.96	3.01	3.939 (3)	164

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

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 $P2_1$ 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: *SET*4 and *CELDIM* in *CAD-4-PC Software*. Data reduction: *DATRD*2 in *NRCVAX*96 (Gabe *et al.*, 1989). Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*b*). Program(s) used to refine structure: *NRCVAX*96 and *SHELXL*97 (Sheldrick, 1997*a*). Molecular graphics: *NRCVAX*96, *ORTEP*II (Johnson, 1976), *PLATON* (Spek, 1997*a*) and *PLUTON* (Spek, 1997*b*). Software used to prepare material for publication: *NRCVAX*96, *SHELXL*97 and *PRPCIF*97 (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.

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1-Phenyltetrazole

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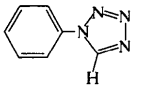
Abstract

The tetrazole ring of the title compound, 1-phenyl-1*H*-1,2,3,4-tetrazole, $C_7H_6N_4$, should be an aromatic system. Slight conjugation effects are present between the phenyl and tetrazole rings. The two rings are not coplanar and have a dihedral angle of 11.8 (1)° between them.

Comment

As part of a study of the aromaticity of tetrazole rings, we are interested in the interaction between tetrazole and phenyl rings. The crystal data of the title compound, (I), was reported by Bryden (1969), but the crystal structure was not determined. We therefore determined the crystal structure of (I) using X-ray crystallographic methods.



(I)

Slight conjugation effects between the phenyl and tetrazole rings are present in (I). The N1—C2 bond length is 1.431 (2) Å, which is almost the same as the normal N—C_{phenyl} single-bond length. Moreover, the tetrazole and phenyl rings are not coplanar [dihedral angle 11.8 (1)°]. These facts indicate that there are slight resonance effects between the two rings.

Ab initio calculations also support the distorted conformation. At the MP2/6-31G* level, the most stable structure has a dihedral angle of 38.6° and is 4.12 kJ mol^{-1} more stable than the coplanar structure. Such a distorted conformation arises due to a steric