Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²)*

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
P	0.42453 (10)	0.22992 (10)	0.09698 (5)	0.0305 (3)
S1	0.66415 (10)	0.20102 (11)	0.05134 (6)	0.0418 (3)
S2	0.8777 (2)	0.3133 (2)	0.00550 (9)	0.0792 (6)
S3	0.90502 (13)	0.08152 (14)	0.05659 (9)	0.0745 (6)
N1	0.7449 (5)	0.3267 (5)	0.0372 (3)	0.081 (2)
N2	0.9576 (4)	0.1903 (5)	0.0196 (2)	0.072 (2)
N3	0.7708 (4)	0.1098 (4)	0.0851 (2)	0.0650 (14)
N4	0.5803 (3)	0.2455 (4)	0.1018 (2)	0.0433 (10)
N5	0.3436 (3)	0.2602 (3)	0.0353 (2)	0.0378 (9)
N6	0.3723 (3)	0.3273 (3)	0.1443 (2)	0.0328 (8)
C1	0.3808 (4)	0.0733 (4)	0.1121 (2)	0.0361 (10)
C2	0.2505 (5)	0.0343 (5)	0.1041 (3)	0.0519 (14)
C3	0.2176 (6)	−0.0844 (5)	0.1173 (3)	0.064 (2)
C4	0.3134 (7)	−0.1643 (6)	0.1382 (3)	0.069 (2)
C5	0.4417 (7)	−0.1276 (5)	0.1480 (3)	0.069 (2)
C6	0.4758 (5)	−0.0090 (4)	0.1340 (2)	0.0469 (13)
C7	0.3196 (7)	0.1712 (6)	−0.0126 (3)	0.058 (2)
C8	0.2708 (10)	0.2431 (8)	−0.0631 (3)	0.087 (2)
C9	0.3419 (13)	0.3649 (9)	−0.0522 (4)	0.113 (4)
C10	0.3425 (10)	0.3843 (6)	0.0101 (3)	0.067 (2)
C11	0.4542 (4)	0.3687 (4)	0.1965 (2)	0.0379 (11)
C12	0.5517 (6)	0.4693 (5)	0.1852 (3)	0.0493 (13)
C13	0.6220 (7)	0.5134 (7)	0.2421 (4)	0.069 (2)
C14	0.6848 (6)	0.4126 (7)	0.2776 (3)	0.068 (2)
C15	0.5879 (6)	0.3125 (7)	0.2889 (3)	0.062 (2)
C16	0.5194 (6)	0.2647 (5)	0.2327 (3)	0.0479 (12)
C17	0.2285 (4)	0.3538 (4)	0.1429 (2)	0.0320 (10)
C18	0.1600 (5)	0.2933 (5)	0.1916 (3)	0.0429 (12)
C19	0.0126 (5)	0.3207 (5)	0.1842 (3)	0.0538 (15)
C20	−0.0149 (6)	0.4568 (6)	0.1818 (3)	0.065 (2)
C21	0.0558 (5)	0.5186 (6)	0.1350 (3)	0.058 (2)
C22	0.2039 (4)	0.4932 (4)	0.1427 (3)	0.0423 (12)

Table 2. *Selected geometric parameters (Å, °)*

P—N4	1.590 (4)	S2—N2	1.583 (6)
P—N5	1.622 (4)	S2—N1	1.599 (5)
P—N6	1.643 (4)	S3—N2	1.579 (6)
P—C1	1.799 (4)	S3—N3	1.597 (5)
S1—N4	1.581 (4)	N6—C11	1.480 (6)
S1—N3	1.622 (4)	N6—C17	1.490 (5)
S1—N1	1.640 (5)		
N4—P—N5	118.1 (2)	S2—N1—S1	118.2 (3)
N4—P—N6	105.1 (2)	S3—N2—S2	123.5 (3)
N5—P—N6	106.8 (2)	S3—N3—S1	118.7 (3)
N4—P—C1	110.4 (2)	S1—N4—P	120.8 (2)
N5—P—C1	104.3 (2)	C10—N5—P	121.5 (4)
N6—P—C1	112.2 (2)	C7—N5—P	124.7 (4)
N4—S1—N3	102.2 (2)	C11—N6—C17	116.4 (3)
N4—S1—N1	101.8 (3)	C11—N6—P	123.3 (3)
N3—S1—N1	106.1 (3)	C17—N6—P	118.8 (3)
N2—S2—N1	114.9 (3)	C6—C1—P	120.3 (3)
N2—S3—N3	114.9 (2)	C2—C1—P	120.7 (3)

All H atoms were located from difference electron density maps.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *CAD-4 Software*. Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: DE1019). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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A Conformationally Restricted Aspartic Acid Analogue

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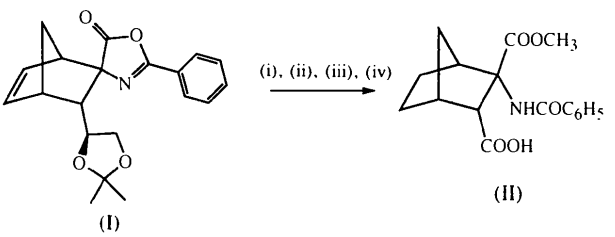
Abstract

In the title compound, (1*R*,2*R*,3*S*,4*S*)-3-benzamido-3-methoxycarbonylbicyclo[2.2.1]heptane-2-carboxylic acid, $C_{17}H_{19}NO_5$, the norbornyl group shows distortion from C_{2v}(*mm*2) symmetry of the parent hydrocarbon. The values determined for the torsion angles about the N—C^{α} (φ) and C^{α}—CO (ψ) bonds correspond to a semi-extended conformation for the amino acid residue. The structure is stabilized by an intermolecular O—H···O hydrogen bond between the carboxy and amide groups and an intramolecular N—H···O hydrogen bond involving the benzamido and the carboxylic acid groups.

Comment

Cyclic non-metabolizable amino acids have useful biological properties; in particular, α-amino acids with a norbornane skeleton have been used to study the transport of amino acids having hydrophobic side chains (Christensen, Handlogten, Lam, Tager & Zand, 1969; Christensen & Cullen, 1969; Tager & Christensen, 1972). Moreover, it has been shown that the incorporation of one or more conformationally constrained amino acids (including cyclic amino acids) into bioactive peptides often gives rise to analogues with enhanced biological activity (Liskamp, 1994; Gante, 1994).

As part of a program aimed at investigating the asymmetric synthesis of α-amino acids having a norbornane skeleton, we have developed a method of obtaining the title amino acid, (II), in diastereomerically pure form, in four steps from the precursor (1*R*,2*S*,3*R*,4*S*)-3-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]bicyclo[2.2.1]-hept-5-ene-2-spiro-4′-[2′-phenyl-5′(4′*H*)-oxazolone], (I) (Buñuel, Cativiela, Díaz-de-Villegas, 1994*a*,*b*), and we describe here the crystal and molecular structure of this new amino acid derivative.



(I) (II)

(i) CH_3ONa/CH_3OH
(ii) H_2, Pd/C
(iii) HCl/CH_3OH
(iv) $NaIO_4$, $RuCl_3.H_2O$

The molecular structure of the aspartic acid analogue (II) is illustrated in Fig. 1. Selected torsion angles are given in Table 2. The values of the bond lengths and angles are in agreement with literature data on the geometry of other norbornane amino acids (Apgar & Ludwig, 1972; Glass, Hojjatie, Sabahi, Steffen & Wilson, 1990).

The asymmetric substitution of the norbornane nucleus often produces a twist about the C1···C4 vector and thereby destroys the C_{2v} symmetry of the bicycloheptane ring system. For the title amino acid derivative, the twist is *S*-(+,+) (Altona & Sundaralingam, 1970). This twisting can be seen from the C1—C2—C3—C4 and C4—C5—C6—C1 torsion angles of 5.5 (3) and 5.0 (4)°, respectively. The two five-membered rings in the norbornane moiety are in envelope conformations. The pseudo-rotation parameters (Rao, Westhof & Sundaralingam, 1981) are P = 300.7° and $\tau(M)$ = 59.8° for the C1, C2, C3, C4, C7 ring, and P = 130.8° and $\tau(M)$ = 59.5° for the C1, C6, C5, C4, C7 ring.

The methyl ester group attached to atom C2 is almost coplanar with the plane defined by the C1, C2 and C8 atoms; the interplanar angle is 6.8 (3)°. The methyl ester group has the C9—O2—C8—C2 sequence in a *trans* disposition [−176.6 (3)°], with the C=O bond pointing away from the bicycloheptane ring.

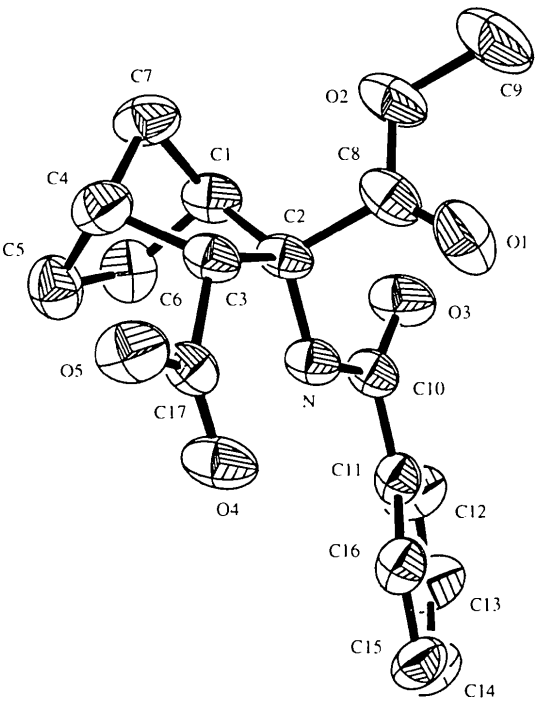


Fig. 1. The molecular structure of (II) showing 50% probability displacement ellipsoids. H atoms are omitted for clarity.

The amino acid derivative (II) is in a semi-extended conformation (IUPAC–IUB Commission on Biochemical Nomenclature, 1970) [C10—N—C2—C8 (φ) −57.7 (3) and N—C2—C8—O2 (ψ) 134.2 (3)°]. The C11—C10—N—C2 (ω) torsion angle is 178.0 (3)°, indicating that the amide linkage adopts the usual *trans* conformation.

The angle between the average planes of the amide and phenyl groups in the benzamido moiety is 26.7 (3)°. The carboxylic acid and amide groups are nearly coplanar, with an angle between them of 9.6 (3)°. This orientation is stabilized by an intramolecular N—H···O4 hydrogen bond involving both groups [H···O4 1.94, N···O4 2.701 (3) Å and N—H···O4 136.0°].

In the crystals of the title compound, rows of molecules are held together along the *a* direction through O_{acid}—H···O=C_{amide} intermolecular hydrogen bonds [H′···O3^{i} 1.75, O5···O3^{i} 2.656 (4) Å and O5—H′···O3^{i} 174.2°; symmetry code: (i) $x+1$, y, z].

Experimental

The title compound was prepared from precursor (I) in four steps (see scheme above): (i) methanolysis with sodium methoxide in methanol for 30 min at room temperature; (ii) hydrogenation of the alkene moiety in the presence of a

catalytic amount of 10% palladium on activated carbon; (iii) hydrolysis of the acetal moiety with 2 *N* hydrochloric acid in methanol; (iv) oxidative cleavage of the diol moiety with an excess of sodium periodate in the presence of ruthenium trichloride. Crystals were obtained by slow evaporation from hexane solution.

Crystal data

$C_{17}H_{19}NO_5$
M_r = 317.33
Monoclinic
$P2_1$
a = 8.314 (3) Å
b = 11.505 (3) Å
c = 8.418 (2) Å
β = 90.25 (2)°
V = 805.2 (4) Å^3
Z = 2
D_x = 1.309 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 39 reflections
θ = 4.92–12.37°
μ = 0.097 mm^{-1}
T = 293 (2) K
Prism
0.42 × 0.38 × 0.22 mm
Colourless

Data collection

Siemens *P*4 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
1970 measured reflections
1622 independent reflections
1382 observed reflections [$I > 2\sigma(I)$]
R_{int} = 0.0155
θ_{max} = 24.97°
$h = -1 \rightarrow 9$
$k = -1 \rightarrow 13$
$l = -10 \rightarrow 10$
3 standard reflections monitored every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.0378
$wR(F^2)$ = 0.0999
S = 1.072
1622 reflections
209 parameters
$w = 1/[\sigma^2(F_o^2) + (0.0534P)^2 + 0.0733P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.016
$\Delta\rho_{max}$ = 0.153 e Å^{-3}
$\Delta\rho_{min}$ = −0.135 e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0301 (56)
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
N	0.3228 (3)	0.5620	0.6795 (3)	0.0415 (6)
O1	0.3008 (3)	0.3442 (4)	0.8238 (3)	0.0736 (8)
O2	0.1670 (3)	0.2892 (3)	0.6052 (3)	0.0650 (7)
O3	0.0546 (2)	0.5492 (3)	0.6981 (3)	0.0626 (7)
O4	0.6459 (2)	0.5782 (3)	0.7055 (3)	0.0571 (7)
O5	0.7937 (2)	0.4420 (3)	0.5891 (3)	0.0592 (7)
C1	0.2633 (3)	0.4681 (4)	0.4147 (4)	0.0473 (8)
C2	0.3363 (3)	0.4567 (4)	0.5859 (4)	0.0394 (7)
C3	0.5186 (3)	0.4248 (4)	0.5469 (3)	0.0402 (7)
C4	0.5249 (4)	0.4352 (4)	0.3624 (4)	0.0518 (9)
C5	0.5002 (4)	0.5637 (5)	0.3150 (4)	0.0574 (9)
C6	0.3171 (4)	0.5826 (5)	0.3418 (4)	0.0576 (10)
C7	0.3633 (4)	0.3820 (4)	0.3168 (4)	0.0568 (10)
C8	0.2658 (4)	0.3580 (4)	0.6860 (5)	0.0501 (9)
C9	0.0891 (5)	0.1974 (5)	0.6980 (7)	0.0854 (15)
C10	0.1803 (3)	0.5996 (4)	0.7326 (4)	0.0416 (7)
C11	0.1804 (3)	0.7074 (4)	0.8330 (3)	0.0421 (7)
C12	0.0439 (4)	0.7777 (4)	0.8322 (4)	0.0610 (10)
C13	0.0416 (4)	0.8807 (5)	0.9151 (5)	0.0694 (12)
C14	0.1758 (4)	0.9155 (4)	1.0027 (4)	0.0603 (10)
C15	0.3088 (4)	0.8461 (5)	1.0086 (4)	0.0561 (10)
C16	0.3135 (4)	0.7414 (4)	0.9236 (3)	0.0470 (8)
C17	0.6544 (3)	0.4914 (4)	0.6235 (3)	0.0388 (7)

Table 2. *Selected torsion angles (°)*

C10—N—C2—C8	−57.7 (3)	C9—O2—C8—C2	−176.6 (3)
C1—C2—C3—C4	5.5 (3)	N—C2—C8—O2	134.2 (3)
C4—C5—C6—C1	5.0 (4)	C2—N—C10—C11	178.0 (3)

H atoms were refined with a riding model, based on initial positions found in a difference synthesis, and with a common U_{iso}. The data do not provide a reliable determination of the absolute configuration [Flack (1983) parameter = 0 (2)].

Data collection: *XSCANS* (Siemens, 1993). Cell refinement: *XSCANS*. Data reduction: *XSCANS*. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *SHELXTL-Plus* (Sheldrick, 1989). Software used to prepare material for publication: *SHELXL*93.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry and torsion angles have been deposited with the IUCr (Reference: CF1044). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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