Scan widths were $(1.20 + 0.35\tan\theta)°$ in ω, with a background/scan time ratio of 0.5. The data were corrected for Lorentz and polarization effects.

The Laue group assignment, systematic absences and intensity statistics consistent with centrosymmetry indicated space group *C*2/*c* (No. 15); since refinement proceeded well, it was adopted. Fourier difference methods were used to locate the H-atom positions. Full-matrix least-squares refinement was performed. In later stages of the refinement, aromatic-ring-H atoms were made canonical: C—H distance = 0.98 Å; U_{iso} = $1.2U_{eq}$ of the attached atom. Atoms H9*A* and H9*B* (on C9*A* and C9*B*) and carboxyl-H atom H_B were refined isotropically.

The *A* molecule carboxyl-O atoms were found to be disordered over two sites, labelled *A* and *A**, with (refined and final) occupancies of 0.66 (2) and 0.34 (2), respectively. Following refinement with all but the two partially occupied carboxylic-H atoms, H_A and H_{A^*}, included in the model, they were assigned fixed coordinates from the resulting Fourier difference map and were assigned a fixed U_{iso} very slightly larger than that of the refined *B* molecule carboxylic-H atom, H_B.

The maximum effect of extinction was 4.7% of F_o for 004. The maximum peak in the final difference map occurred ~1.2 Å from O1*A** and O2*A*, but was not suitably oriented to be assigned as a potential partial-occupancy carboxylic-H atom; the minimum peak occurred near the center of one of the benzenoid rings of the *B* molecule.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1989). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *TEXSAN*. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *TEXSAN*.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: BK1245). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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A New Conformationally Restricted Aspartic Acid Analogue with a Cyclohexanone Skeleton

ELENA BUÑUEL, CARLOS CATIVIELA, MARÍA D. DÍAZ-DE-VILLEGAS AND JOSÉ A. GÁLVEZ

Departamento de Química Orgánica, Instituto de Ciencia de Materiales de Aragón, Universidad de Zaragoza-CSIC, 50009 Zaragoza, Spain. E-mail: cativiela@posta.unizar.es

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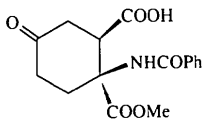
Abstract

In the compound (1*R*,2*S*)-2-benzamido-2-methoxycarbonyl-5-oxocyclohexane-1-carboxylic acid, $C_{16}H_{17}NO_6$, the cyclohexanone ring adopts a distorted chair conformation. The carboxylic acid and the methyl ester groups occupy the axial positions, while the benzamido group is equatorial. 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 crystal structure is stabilized by two intermolecular hydrogen bonds (O—H···O and N—H···O) involving the carboxylic acid, the benzamido and the methyl ester groups.

Comment

The use of uncommon amino acid residues in the synthesis of peptides with restricted conformational flexibility has acquired increasing importance in the design of specifically folded analogues of biologically active

peptides (Liskamp, 1994; Gante, 1994). In this context, we have developed a new methodology for the stereoselective synthesis of new non-proteinogenic conformationally restricted α-amino acids that involves the use of (*Z*)-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethylidene]-2-phenyl-5(4*H*)-oxazolone as a dienophile in Diels–Alder reactions with different dienes (Buñuel, Cativiela & Díaz-de-Villegas, 1994, 1995, 1996; Buñuel, Cativiela, Díaz-de-Villegas & Garcia, 1994) and, as part of our investigations of the conformational properties of some of these interesting compounds (Buñuel, Cativiela, Díaz-de-Villegas & Gálvez, 1996*a*,*b*), we describe here the crystal and molecular structure of a new conformationally restricted aspartic acid analogue with a cyclohexanone skeleton, (I).



(I)

A perspective view of (I) with the numbering scheme used in this analysis is shown in Fig. 1. The cyclohexanone ring adopts a distorted chair conformation [the Cremer & Pople (1975) puckering parameters are Q = 0.497 (2) Å and θ = 10.1 (2)°] in which the C1 and C4 atoms are displaced from the plane defined by the other four atoms by 0.592 (2) and −0.547 (2) Å, respectively. As for the torsion angles relating the cyclohexane ring to the substituents, the (+*sc*,−*sc*) conformation (axial disposition) is adopted by the carboxylic acid and methyl ester groups, while the (*ap*,*ap*) conformation (equatorial disposition) is adopted by the benzamido group.

The methyl ester group attached to atom C1 is planar and adopts a nearly eclipsed conformation with respect to the C1—C2 bond of the cyclohexane ring [the torsion angle C2—C1—C7—O3 is −12.0 (2)°].

The angle between the average planes of the amide and phenyl groups in the benzamido moiety is 33.8 (1)°.

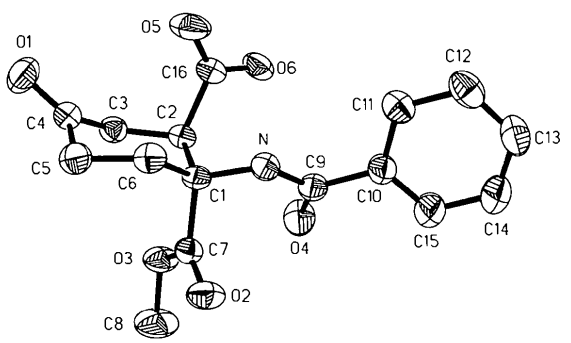


Fig. 1. The molecular structure of (I) showing 50% probability displacement ellipsoids. H atoms have been omitted for clarity.

The amide linkage is found in the usual *trans* conformation [the torsion angle C1—N—C9—C10 is 174.8 (2)°] and adopts an antiperiplanar conformation with respect to the C1—C6 bond of the cyclohexane ring [the torsion angle C9—N—C1—C6 is 169.7 (2)°]. The torsion angle C1—C2—C16—O5 of −72.9 (2)° indicates that the axial carboxylic acid group is conveniently orientated in a conformation that avoids an eclipsing of the C2—C3 and C16—O5 bonds.

The amino acid residue adopts a semi-extended conformation; the values of the backbone torsion angles C9—N—C1—C7 [φ = 53.5 (2)°] and N—C1—C7—O3 [ψ = −132.4 (2)°] (IUPAC–IUB Commission on Biochemical Nomenclature, 1970) fall in the F^* region of the conformational map (Zimmerman, Pottle, Nemethy & Scheraga, 1977). The values of the torsion angles N—C1—C2—C3 [χ^{11} = −163.9 (1)°] and N—C1—C6—C5 [χ^{12} = 172.3 (2)°] relating the peptide chain to the cyclohexane ring reflect an (*ap*,*ap*) conformation.

In the crystal, the molecules form an infinite layer perpendicular to the crystallographic z axis (Fig. 2), characterized by two different intermolecular hydrogen bonds, *i.e.* an (amide)N—H···O=C(methyl ester) and an (acid)O—H···O=C(amide) hydrogen bond [N···O2^{i} 3.003 (2), H···O2^{i} 2.09 Å and N—H···O2^{i} 176°; O6···O4^{ii} 2.597 (2), HO···O4^{ii} 1.794 (2) Å and O6—HO···O4^{ii} 150°; symmetry codes: (i) $1-x$, $-\frac{1}{2}+y$, $\frac{1}{2}-z$; (ii) $2-x$, $-\frac{1}{2}+y$, $\frac{1}{2}-z$]. The layers are held together by van der Waals forces between the phenyl groups.

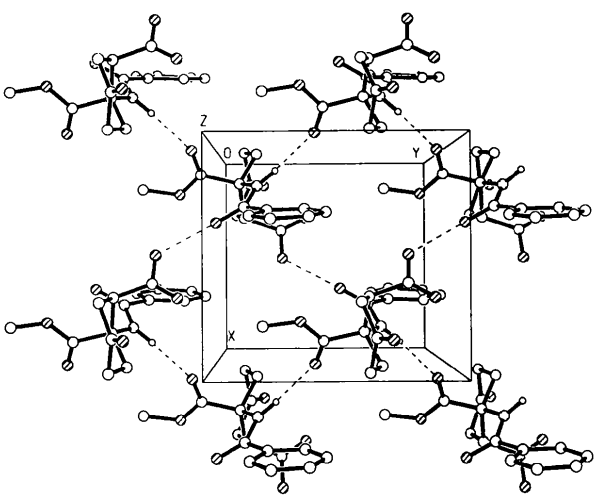


Fig. 2. Packing diagram viewed down the crystallographic z axis; O—H···O and N—H···O hydrogen bonds are shown as dashed lines.

Experimental

The title compound was prepared according to a procedure described by Buñuel, Cativiela & Díaz-de-Villegas (1996).

Crystals were obtained by slow evaporation from a hexane solution.

Crystal data

$C_{16}H_{17}NO_6$
M_r = 319.31
Orthorhombic
$P2_12_12_1$
a = 8.707 (1) Å
b = 9.313 (1) Å
c = 19.869 (1) Å
V = 1611.1 (3) Å^3
Z = 4
D_x = 1.316 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 32 reflections
θ = 3.80–12.49°
μ = 0.102 mm^{-1}
T = 293 (2) K
Prism
0.68 × 0.60 × 0.38 mm
Colourless

Data collection

Siemens $P4$ diffractometer
$\theta/2\theta$ scans
Absorption correction: none
2219 measured reflections
2042 independent reflections
1917 observed reflections [$I > 2\sigma(I)$]
R_{int} = 0.0169

θ_{max} = 25°
$h = -1 \rightarrow 10$
$k = -1 \rightarrow 11$
$l = -1 \rightarrow 23$
3 standard reflections monitored every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.0321
$wR(F^2)$ = 0.0871
S = 1.063
2042 reflections
209 parameters
Only U_{iso} refined for each H atom
$w = 1/[\sigma^2(F_o^2) + (0.05P)^2 + 0.1993P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.157 e Å^{-3}
$\Delta\rho_{min}$ = −0.167 e Å^{-3}

Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Absolute configuration: assigned on the basis of the known configuration of the (*Z*)-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethylidene]-2-phenyl-5(4*H*)-oxazolone reagent

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

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

	x	y	z	U_{eq}
N	0.6925 (2)	0.3084 (2)	0.25896 (7)	0.0339 (3)
O1	0.6665 (2)	0.2918 (2)	0.52787 (7)	0.0587 (5)
O2	0.5351 (2)	0.5743 (2)	0.27031 (7)	0.0473 (4)
O3	0.7228 (2)	0.63323 (14)	0.34254 (7)	0.0475 (4)
O4	0.8562 (2)	0.4711 (2)	0.21835 (8)	0.0545 (4)
O5	0.8262 (2)	0.1110 (2)	0.38483 (9)	0.0582 (4)
O6	1.0080 (2)	0.2061 (2)	0.31920 (8)	0.0508 (4)
C1	0.6767 (2)	0.3829 (2)	0.32356 (9)	0.0302 (4)
C2	0.8285 (2)	0.3660 (2)	0.36456 (9)	0.0306 (4)
C3	0.8115 (2)	0.4022 (2)	0.44029 (9)	0.0360 (4)
C4	0.6672 (2)	0.3466 (2)	0.47215 (9)	0.0386 (4)
C5	0.5229 (2)	0.3693 (2)	0.43263 (10)	0.0430 (5)
C6	0.5389 (2)	0.3149 (2)	0.36021 (10)	0.0376 (4)
C7	0.6375 (2)	0.5416 (2)	0.30784 (9)	0.0338 (4)
C8	0.7010 (4)	0.7841 (2)	0.3276 (2)	0.0734 (9)
C9	0.7873 (2)	0.3571 (2)	0.21086 (9)	0.0367 (4)
C10	0.8052 (3)	0.2656 (2)	0.14915 (10)	0.0420 (5)
C11	0.8003 (2)	0.1169 (2)	0.15274 (11)	0.0426 (5)
C12	0.8174 (2)	0.0359 (3)	0.09484 (12)	0.0494 (5)
C13	0.8384 (4)	0.1018 (3)	0.03411 (12)	0.0707 (8)
C14	0.8482 (6)	0.2490 (4)	0.03095 (13)	0.104 (2)
C15	0.8314 (5)	0.3311 (3)	0.08858 (12)	0.0815 (11)
C16	0.8855 (2)	0.2126 (2)	0.35769 (10)	0.0363 (4)

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

N—C9	1.342 (2)	C2—C16	1.519 (3)
N—C1	1.465 (2)	C2—C3	1.549 (3)
O1—C4	1.219 (2)	C3—C4	1.499 (3)
O2—C7	1.202 (2)	C4—C5	1.497 (3)
O3—C7	1.325 (2)	C5—C6	1.532 (3)
O3—C8	1.449 (3)	C9—C10	1.501 (3)
O4—C9	1.229 (2)	C10—C15	1.368 (3)
O5—C16	1.205 (2)	C10—C11	1.387 (3)
O6—C16	1.314 (2)	C11—C12	1.384 (3)
C1—C6	1.540 (3)	C12—C13	1.366 (4)
C1—C7	1.549 (2)	C13—C14	1.375 (4)
C1—C2	1.560 (3)	C14—C15	1.385 (4)
C9—N—C1	121.44 (15)	O2—C7—O3	125.2 (2)
C7—O3—C8	116.4 (2)	O2—C7—C1	122.0 (2)
N—C1—C6	107.03 (14)	O3—C7—C1	112.72 (15)
N—C1—C7	107.21 (14)	O4—C9—N	120.4 (2)
C6—C1—C7	108.4 (2)	O4—C9—C10	122.6 (2)
N—C1—C2	109.28 (14)	N—C9—C10	117.0 (2)
C6—C1—C2	111.83 (14)	C15—C10—C11	119.7 (2)
C7—C1—C2	112.81 (14)	C15—C10—C9	118.9 (2)
C16—C2—C3	108.9 (2)	C11—C10—C9	121.4 (2)
C16—C2—C1	108.95 (15)	C12—C11—C10	119.9 (2)
C3—C2—C1	113.9 (2)	C13—C12—C11	120.2 (2)
C4—C3—C2	114.5 (2)	C12—C13—C14	119.8 (2)
O1—C4—C5	122.1 (2)	C13—C14—C15	120.4 (3)
O1—C4—C3	122.1 (2)	C10—C15—C14	119.9 (3)
C5—C4—C3	115.68 (15)	O5—C16—O6	124.9 (2)
C4—C5—C6	111.7 (2)	O5—C16—C2	123.9 (2)
C5—C6—C1	112.3 (2)	O6—C16—C2	111.2 (2)
C9—N—C1—C6	169.7 (2)	C7—C1—C6—C5	−72.4 (2)
C9—N—C1—C7	53.5 (2)	C8—O3—C7—C1	176.0 (2)
C6—C1—C2—C16	76.2 (2)	N—C1—C7—O3	−132.4 (2)
N—C1—C2—C3	−163.9 (1)	C2—C1—C7—O3	−12.0 (2)
C7—C1—C2—C3	77.0 (2)	C1—N—C9—C10	174.8 (2)
C16—C2—C3—C4	−80.2 (2)	C1—C2—C16—O5	−72.9 (2)
N—C1—C6—C5	172.3 (2)		

Data collection: *XSCANS* (Siemens, 1993). Cell refinement: *XSCANS*. Data reduction: *XSCANS*. Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1992). 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. Molecular geometry calculations: *PARST* (Nardelli, 1983).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1251). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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