C1—C2	1.384 (4)	C11—C12	1.495 (4)
C2—C3	1.385 (4)	C12—C13	1.490 (4)
C3—C4	1.381 (4)	C14—O2	1.199 (4)
C4—C5	1.375 (5)	C14—O3	1.317 (4)
C4—C7	1.510 (4)	O3—C15	1.450 (4)
C5—C6	1.386 (4)	C15—C16	1.416 (6)
C8—C13	1.323 (4)		
O1—S—C8	106.89 (13)	C13—C8—S	118.0 (2)
O1—S—C1	106.42 (14)	C9—C8—S	117.2 (2)
C8—S—C1	98.50 (11)	C10—C9—C8	111.7 (2)
C6—C1—C2	120.1 (2)	C11—C10—C9	124.1 (3)
C6—C1—S	118.9 (2)	C10—C11—C14	121.7 (3)
C2—C1—S	120.8 (2)	C10—C11—C12	123.1 (2)
C1—C2—C3	119.1 (3)	C14—C11—C12	115.2 (2)
C4—C3—C2	121.9 (3)	C13—C12—C11	112.8 (2)
C5—C4—C3	117.8 (3)	C8—C13—C12	122.9 (3)
C5—C4—C7	121.7 (3)	O2—C14—O3	123.3 (3)
C3—C4—C7	120.5 (3)	O2—C14—C11	123.2 (3)
C4—C5—C6	121.8 (3)	O3—C14—C11	113.4 (3)
C1—C6—C5	119.3 (3)	C14—O3—C15	118.6 (3)
C13—C8—C9	124.6 (2)	C16—C15—O3	109.0 (3)

The absolute configuration was assigned to agree with the known chirality of the sulfoxide group as established by the synthesis of (1) (Bonfand, Gosselin & Maignan, 1992) and the method described by Flack (1983) was used to confirm the absolute configuration $\chi = 0.33\,(11)$ [compared to $\chi = 0.67\,(11)$ for the inverted absolute structure (*SHELXL*93 option applied on non-centrosymmetric space groups)]. H atoms were refined as rigid groups with their neighbours using *AFIX* in *SHELXL*93 (Sheldrick, 1993).

Data collection: *DIF*4 (Stoe & Cie, 1988*a*). Cell refinement: *DIF*4. Data reduction: *REDU*4 (Stoe & Cie, 1988*b*). Program(s) used to solve structure: *PATT SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP* (Johnson, 1965).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: PA1227). 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 Bicyclo-[2.2.2]octane Skeleton

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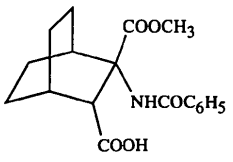
Abstract

The bicyclo[2.2.2]octane cage in (2*R*,3*S*)-3-benzamido-3-methoxycarbonylbicyclo[2.2.2]octane-2-carboxylic acid, $C_{18}H_{21}NO_5$, has approximate D_3 symmetry and the three six-membered rings of this fragment all deviate slightly from ideal boat conformations. The values determined for the torsion angles about the N—Cα (φ) and Cα—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

Whereas the synthesis of amino acids has been a matter of longstanding interest (Duthaler, 1994; Williams, 1989), the synthesis of conformationally constrained amino acids has only attracted significant attention in the past decade when it has been recognized that their incorporation into peptides is a powerful approach for generating structurally defined peptides as conformational probes and bioactive agents (Liskamp, 1994; Gante, 1994). In this context, and as part of our research project on the stereoselective synthesis of new non-proteinogenic and unusual conformationally restricted amino acids, we have developed a new methodology involving the use of *Z*-2-phenyl-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethylen]-5(4*H*)-oxazolone as dienophile in Diels–Alder reactions with different dienes allowing the synthesis of new and interesting compounds (Buñuel, Cativiela & Díaz-de-Villegas, 1994, 1995; Buñuel, Cativiela, Díaz-de-Villegas & Garcia, 1994.

In a previous paper, we reported the crystal structure of an aspartic acid analogue with a norbornyl skeleton (Buñuel, Cativiela, Díaz-de-Villegas & Gálvez, 1996), and now we describe here the crystal and molecular structure of another conformationally restricted aspartic acid analogue (I) with a bicyclo[2.2.2]octane skeleton.



(I)

The bicyclo[2.2.2]octane fragment has approximate D_3 symmetry, but the presence of substituents, and the resulting steric overcrowding, leads to some significant deviations from the ideal symmetry. This can be seen in the torsion angles (Table 2) or the puckering parameters (Cremer & Pople, 1975). All three six-membered rings adopt distorted boat conformations: Q = 0.876 (4) Å, θ = 90.0 (3), φ = −172.1 (3)° for the C1,C2,C3,C4,C5,C6 ring; Q = 0.845 (4) Å, θ = 90.7 (3), φ = −9.1 (3)° for the C1,C7,C8,C4,C5,C6 ring; Q = 0.823 (4) Å, θ = 89.0 (3), φ = −9.6 (3)° for the C1,C2,C3,C4,C8,C7 ring.

The amino acid residue in (I) corresponds to a semi-extended conformation in a polypeptide chain (IUPAC–IUB Commission on Biochemical Nomenclature, 1970) [C11—N—C2—C9 (φ) = 55.4 (4) and N—C2—C9—O2 (ψ) = −132.8 (3)°]. The C2—N—C11—C12 (ω) torsion angle is 172.0 (3)° indicating that the amide linkage adopts the usual *trans* conformation.

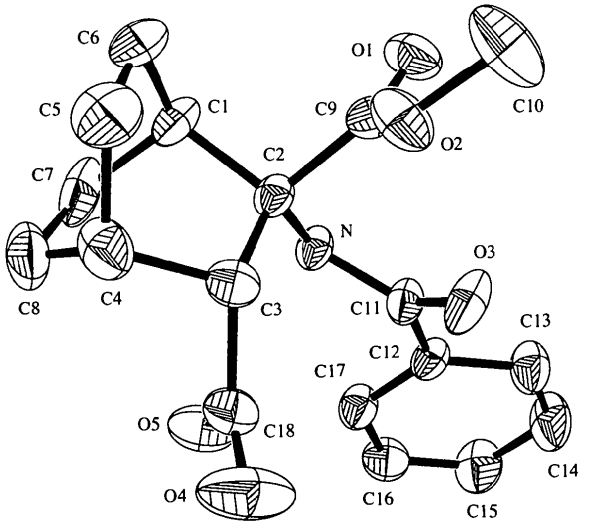


Fig. 1. The molecular structure of (I) showing 50% probability displacement ellipsoids. H atoms are omitted for clarity.

The crystal structure is stabilized by two intermolecular hydrogen bonds (O—H···O and N—H···O) involving the carboxylic acid and the benzamido groups, and the benzamido and methyl ester groups, respectively [O5···O3^{i} 2.607 (4), N···O1^{ii} 3.033 (4) Å; symmetry codes: (i) $-x$, $\frac{1}{2}+y$, $1-z$; (ii) $1-x$, $\frac{1}{2}+y$, $1-z$]. The hydrogen-bonded molecules form an infinite layer perpendicular to the crystallographic c axis. The layers are held together by means of van der Waals forces involving the phenyl and bicyclo[2.2.2]octane groups.

Experimental

The title compound was prepared from (1*S*,2*S*,3*R*,4*R*)-3-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]bicyclo[2.2.2]oct-5-en-2-spiro{4′-[2′-phenyl-5′(4′*H*)-oxazolone]} (Buñuel, Cativiela & Díaz-de-Villegas, 1995) in four steps: (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 2N hydrochloric acid in methanol, and (iv) oxidative cleavage of diol moiety with an excess of sodium periodate in the presence of ruthenium trichloride. Crystals were obtained by slow evaporation from a hexane solution.

Crystal data

$C_{18}H_{21}NO_5$
M_r = 331.36
Monoclinic
$P2_1$
a = 8.248 (3) Å
b = 9.593 (3) Å
c = 10.943 (3) Å
β = 99.480 (10)°
V = 854.0 (5) Å^3
Z = 2
D_x = 1.289 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 38 reflections
θ = 5.25–12.55°
μ = 0.094 mm^{-1}
T = 293 (2) K
Prism
0.62 × 0.58 × 0.08 mm
Colourless

Data collection

Siemens *P*4 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
2161 measured reflections
1778 independent reflections
1423 observed reflections [$I > 2\sigma(I)$]
R_{int} = 0.0613
θ_{max} = 25.09°
$h = -1 \rightarrow 9$
$k = -1 \rightarrow 11$
$l = -13 \rightarrow 12$
3 standard reflections monitored every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.0440
$wR(F^2)$ = 0.1134
S = 1.062
1778 reflections
218 parameters
Only H-atom U's refined
$w = 1/[\sigma^2(F_o^2) + (0.0577P)^2 + 0.0358P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = −0.001
$\Delta\rho_{max}$ = 0.202 e Å^{-3}
$\Delta\rho_{min}$ = −0.206 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: Flack (1983)
Flack parameter = −1.3 (19)

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	0.3241 (3)	0.2194 (3)	0.5179 (2)	0.0285 (6)
O1	0.5014 (3)	−0.0295 (3)	0.5678 (2)	0.0463 (7)
O2	0.3395 (3)	−0.0709 (3)	0.7103 (3)	0.0490 (7)
O3	0.1406 (3)	0.0476 (3)	0.4776 (2)	0.0473 (8)
O4	−0.0440 (3)	0.2635 (4)	0.7141 (4)	0.0796 (12)

O5	0.1102 (3)	0.3907 (3)	0.6088 (2)	0.0480 (7)
C1	0.5332 (4)	0.2431 (4)	0.7075 (4)	0.0416 (10)
C2	0.3712 (4)	0.1698 (3)	0.6471 (3)	0.0274 (8)
C3	0.2362 (4)	0.1986 (4)	0.7313 (3)	0.0336 (8)
C4	0.3193 (5)	0.2694 (5)	0.8541 (4)	0.0496 (10)
C5	0.4623 (6)	0.1742 (6)	0.9150 (4)	0.0632 (14)
C6	0.5955 (5)	0.1709 (5)	0.8338 (4)	0.0569 (13)
C7	0.5011 (5)	0.3970 (5)	0.7307 (4)	0.0560 (12)
C8	0.3897 (6)	0.4107 (5)	0.8307 (4)	0.0616 (13)
C9	0.4094 (4)	0.0125 (4)	0.6350 (3)	0.0346 (9)
C10	0.3632 (7)	−0.2193 (5)	0.6982 (5)	0.077 (2)
C11	0.2021 (4)	0.1563 (4)	0.4427 (3)	0.0303 (8)
C12	0.1412 (4)	0.2192 (4)	0.3182 (3)	0.0314 (8)
C13	0.0822 (5)	0.1301 (5)	0.2189 (3)	0.0415 (10)
C14	0.0142 (6)	0.1863 (5)	0.1038 (4)	0.0523 (11)
C15	0.0015 (5)	0.3291 (5)	0.0878 (3)	0.0487 (11)
C16	0.0602 (4)	0.4186 (5)	0.1848 (3)	0.0411 (9)
C17	0.1297 (4)	0.3636 (4)	0.3003 (3)	0.0351 (9)
C18	0.0853 (4)	0.2843 (4)	0.6803 (3)	0.0393 (9)

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

N—C11	1.335 (4)	C2—C3	1.582 (5)
N—C2	1.481 (4)	C3—C4	1.560 (6)
C1—C7	1.529 (7)	C4—C8	1.513 (7)
C1—C6	1.555 (6)	C4—C5	1.552 (6)
C1—C2	1.558 (4)	C5—C6	1.522 (6)
C2—C9	1.552 (5)	C7—C8	1.545 (6)
C11—N—C2	119.7 (3)	C9—C2—C3	113.0 (3)
C9—O2—C10	116.9 (3)	C1—C2—C3	108.1 (3)
C7—C1—C6	108.9 (4)	C18—C3—C4	107.3 (3)
C7—C1—C2	110.3 (3)	C18—C3—C2	119.5 (3)
C6—C1—C2	108.1 (3)	C4—C3—C2	109.0 (3)
N—C2—C9	104.8 (3)	C8—C4—C5	108.3 (4)
N—C2—C1	109.4 (3)	C8—C4—C3	111.7 (3)
C9—C2—C1	107.6 (3)	C5—C4—C3	108.0 (4)
N—C2—C3	113.6 (3)		
C11—N—C2—C9	55.4 (4)	C1—C2—C9—O1	−65.7 (4)
C11—N—C2—C1	170.6 (3)	C3—C2—C9—O1	175.1 (3)
C11—N—C2—C3	−68.5 (4)	N—C2—C9—O2	−1328 (3)
C1—C2—C3—C4	−8.7 (4)	C3—C2—C9—O2	−8.5 (4)
C4—C5—C6—C1	−9.2 (6)	C2—N—C11—O3	−7.4 (5)
C1—C7—C8—C4	−11.8 (5)	C2—N—C11—C12	172.0 (3)
C10—O2—C9—O1	−7.0 (6)	N—C11—C12—C17	−37.1 (5)
C10—O2—C9—C2	176.6 (4)	N—C11—C12—C13	147.9 (3)
N—C2—C9—O1	50.8 (4)	C2—C3—C18—O4	149.4 (4)

Data collection: *XSCANS* (Siemens, 1994). 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. Geometrical calculations: *PARST* (Nardell, 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: HA1159). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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[3-(4-Methylphenyl)-5-isoxazolyl]acetonitrile

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Abstract

An improved synthesis of the title compound, $C_{12}H_{10}N_2O$, *via* the reaction of 6-(4-methylphenyl)-4-methylthio-2-oxo-2*H*-pyran-3-carbonitrile and hydroxylamine hydrochloride in pyridine is reported. The isoxazole ring is planar and is inclined at an angle of 34.2 (1)° with respect to the aromatic ring. All bond lengths and angles are unexceptional.

Comment

Isoxazoles are known to possess a range of biological activities, a particularly important example being antispasmodic activity (Naruto *et al.*, 1982, 1983). In this context, an interesting reaction has recently been reported (Ram, Hussaini, Singh & Shoeb, 1993) in which three different compounds [(II)–(IV)] having an isoxazole moiety are obtained in one step by the treatment of 6-(4-methylphenyl)-4-methylthio-