

For all compounds, data collection: *AFC/MSD Diffractometer Control System* (Rigaku Corporation, 1993); cell refinement: *AFC/MSD Diffractometer Control System*; data reduction: local programs; program(s) used to solve structure: *CRYSTAN-GM* (Edwards, Gilmore, Mackay & Stewart, 1995); program(s) used to refine structure: *CRYSTAN-GM*; molecular graphics: *CRYSTAN-GM*; software used to prepare material for publication: *CRYSTAN-GM*.

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Lists of atomic coordinates, displacement parameters, structure factors and complete geometry have been deposited with the IUCr (Reference: OA1018). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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1 α ,5 α -Dihydroxymanoyl Oxide, a Novel Diterpene from *Satureja gilliesii*

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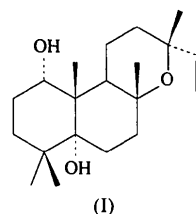
(Received 27 February 1995; accepted 2 January 1997)

Abstract

The structure of the title diterpene, C₂₀H₃₄O₃ (8 α ,13R-epoxylabd-14-ene-1 α ,5 α -diol), exhibits a very uncommon oxidation pattern, with two axially disposed hydroxyl substituents at C1 and C5, and five tertiary methyl groups.

Comment

The title compound, (I), was isolated, along with other diterpenoids, from the aerial parts of *Satureja gilliesii* (Labiatae), a small shrub endemic to central Chile. This species and other members of the genus display an uncommon natural resistance to insect attack (Lincoln & Lagenheim, 1981; Montenegro, Jordán & Aljaro, 1980). The chemical studies on the genus have been restricted to mainly the essential oil contents (Navarro, Zarzuelo, Jiménez & Duarte, 1989; Lincoln & Lagenheim, 1981), thus, it was of interest to investigate the other constituents of the extract in order to identify the metabolites responsible for the antifeedant behaviour of *S. gilliesii*. The isolation of some rare mono- and sesquiterpenoids from this species have been reported previously (Manríquez, Labbé, Castillo, von Schnering & Peters, 1990; Labbé, Castillo & Connolly, 1993).



The combined spectroscopic data of the title compound revealed a manoyl oxide diterpene derivative, with five tertiary methyl groups and two hydroxyl substituents (one secondary and one tertiary). However, the hydroxyl groups could not be located unequivocally from the spectroscopic data alone. The present single-crystal X-ray analysis establishes the molecular structure of this compound as shown in Fig. 1.

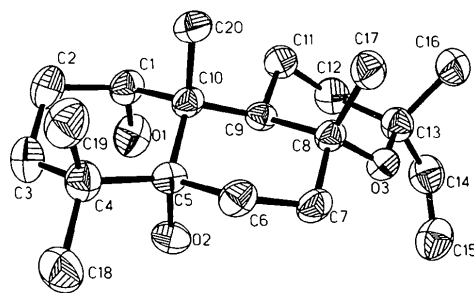


Fig. 1. A perspective drawing of the title molecule with H atoms omitted, displacement ellipsoids at the 50% probability level and atom site labels.

The three fused six-membered rings have a chair conformation; both hydroxyl substituents, α -secondary at C1 and α -tertiary at C5, are axially disposed on one side of the molecule and four of the five methyl groups are axially disposed on the other side, giving

rise to a number of 1,3-diaxial interactions. All observed bond lengths and angles are within expected ranges. However, the distances between the axial methyl groups [C16...C17 3.169 (5), C17...C20 3.101 (5) and C20...C19 3.153 (5) Å] are all shorter than the values reported by Escobar & Wittke (1984, 1988) for drimenol, isodrimenin and some related products that show similar steric hindrance. No intermolecular hydrogen-bonding interactions were detected, but the O2—H102...O1 and O1—H01...O2 intramolecular interactions are possible hydrogen bonds. The absolute configuration of the molecule could not be established from this X-ray analysis, but Fig. 1 shows the one assumed by Labbé, Castillo, Faini, Coll & Connolly (1994) to agree with their chemical and spectroscopic studies of this compound and the other diterpenoids obtained from *S. gilliesii*.

Experimental

The title compound was extracted with CH₂Cl₂ from fresh flowering plant tops. Isolation was achieved using repeated flash chromatography. Crystals of the title compound were obtained from a chloroform/hexane solution.

Crystal data

C ₂₀ H ₃₄ O ₃	Mo K α radiation
$M_r = 322.5$	$\lambda = 0.71073$ Å
Monoclinic	Cell parameters from 19 reflections
$P2_1$	$\theta = 7.5\text{--}15.0^\circ$
$a = 8.467$ (2) Å	$\mu = 0.077$ mm ⁻¹
$b = 11.154$ (2) Å	$T = 295$ K
$c = 9.654$ (2) Å	Prism
$\beta = 92.24$ (2) $^\circ$	$0.80 \times 0.26 \times 0.15$ mm
$V = 911.0$ (3) Å ³	Colourless
$Z = 2$	
$D_x = 1.176$ Mg m ⁻³	
D_m not measured	

Data collection

Siemens R3m/V diffractometer	$R_{\text{int}} = 0.01$
$2\theta/\theta$ scans	$\theta_{\text{max}} = 27.5^\circ$
Absorption correction: none	$h = 0 \rightarrow 11$
2352 measured reflections	$k = 0 \rightarrow 14$
2208 independent reflections	$l = -12 \rightarrow 12$
1745 reflections with $F > 4\sigma(F)$	3 standard reflections every 48 reflections
	intensity decay: none

Refinement

Refinement on F	$(\Delta/\sigma)_{\text{max}} = 0.010$
$R = 0.0380$	$\Delta\rho_{\text{max}} = 0.19$ e Å ⁻³
$wR = 0.0423$	$\Delta\rho_{\text{min}} = -0.14$ e Å ⁻³
$S = 1.24$	Extinction correction: none
1745 reflections	Scattering factors from <i>International Tables for Crystallography</i> (Vol. C)
309 parameters	
H atoms: see below	
$w = 1/[\sigma^2(F) + 0.0005F^2]$	

Table 1. Selected geometric parameters (Å, $^\circ$)

O1—C1	1.432 (4)	C6—C7	1.533 (4)
O2—C5	1.452 (3)	C7—C8	1.527 (5)
O3—C8	1.456 (3)	C8—C9	1.534 (4)
O3—C13	1.431 (4)	C8—C17	1.539 (4)
C1—C2	1.524 (4)	C9—C10	1.561 (4)
C1—C10	1.548 (4)	C9—C11	1.531 (5)
C2—C3	1.514 (6)	C10—C20	1.545 (4)
C3—C4	1.530 (5)	C11—C12	1.520 (4)
C4—C5	1.573 (4)	C12—C13	1.539 (5)
C4—C18	1.537 (6)	C13—C14	1.504 (5)
C4—C19	1.537 (5)	C13—C16	1.540 (4)
C5—C6	1.529 (5)	C14—C15	1.298 (6)
C5—C10	1.573 (5)		
C8—O3—C13	120.2 (3)	C7—C8—C9	109.3 (2)
O1—C1—C2	110.3 (2)	O3—C8—C17	109.5 (2)
O1—C1—C10	111.8 (2)	C7—C8—C17	108.7 (2)
C2—C1—C10	112.7 (2)	C9—C8—C17	117.0 (3)
C1—C2—C3	112.9 (3)	C8—C9—C10	115.0 (2)
C2—C3—C4	114.7 (3)	C8—C9—C11	109.3 (2)
C3—C4—C5	108.2 (3)	C10—C9—C11	117.2 (3)
C3—C4—C18	107.2 (3)	C1—C10—C5	109.6 (2)
C5—C4—C18	110.2 (3)	C1—C10—C9	110.6 (2)
C3—C4—C19	110.3 (3)	C5—C10—C9	106.9 (3)
C5—C4—C19	114.0 (2)	C1—C10—C20	105.0 (3)
C18—C4—C19	106.8 (3)	C5—C10—C20	114.4 (2)
O2—C5—C6	105.6 (2)	C9—C10—C20	110.3 (2)
O2—C5—C10	105.2 (3)	C9—C11—C12	107.2 (3)
C4—C5—C6	113.7 (2)	C11—C12—C13	114.0 (3)
O2—C5—C10	107.5 (2)	O3—C13—C12	111.6 (2)
C4—C5—C10	114.8 (3)	O3—C13—C14	105.6 (3)
C6—C5—C10	109.3 (2)	C12—C13—C14	108.6 (3)
C5—C6—C7	112.2 (2)	O3—C13—C16	111.5 (3)
C6—C7—C8	113.7 (3)	C12—C13—C16	111.8 (3)
O3—C8—C7	103.4 (3)	C14—C13—C16	107.3 (3)
O3—C8—C9	108.1 (2)	C13—C14—C15	126.6 (3)

All H atoms were located from difference Fourier maps and refined with fixed isotropic U values equal to those of the bonded C or O atoms.

Data collection: *P3/P4-PC Diffractometer Program* (Siemens, 1991). Cell refinement: *P3/P4-PC Diffractometer Program*. Data reduction: *XDISK* in *SHELXTL/PC* (Sheldrick, 1990). Program(s) used to solve structure: *XS* in *SHELXTL/PC*. Program(s) used to refine structure: *XLS* in *SHELXTL/PC*. Molecular graphics: *XP* in *SHELXTL/PC*. Software used to prepare material for publication: *XPUBL* in *SHELXTL/PC*.

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Lists of atomic coordinates, displacement parameters, structure factors and complete geometry have been deposited with the IUCr (Reference: SX1001). 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 with a Norbornane Skeleton. II

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Abstract

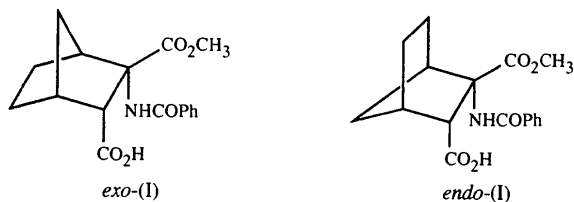
In (1*S*,2*R*,3*S*,4*R*)-3-benzamido-3-methoxycarbonylbicyclo[2.2.1]heptane-2-carboxylic acid, C₁₇H₁₉NO₅, the values determined for the torsion angles about the N—C_α(φ) and C_α—CO(ψ) bonds correspond to a semi-extended conformation of the amino acid residue. The crystal structure is stabilized by two intermolecular hydrogen bonds (O—H···O and N—H···O) involving the benzamido, carboxylic acid and methyl ester groups.

Comment

The introduction of non-natural amino acids into biologically active peptides has become one of the most powerful tools for studying the properties of such peptides (Gante, 1994; Liskamp, 1994). Specific structural, stereoelectronic, steric and conformational properties can be examined by proper design of such peptides. For some years, we have been focusing our attention on those amino acids that introduce specific conformational and topographical modifications to their side chains because of the significant changes in potency, receptor selectivity and biostability that can result when they are incorporated into bioactive peptides. Some chain-modification strategies have concentrated on conformational restrictions induced by (a) increased steric bulk and (b) cyclization of the side-chain atoms with the main-chain atoms.

Non-proteinogenic α,α -disubstituted α -amino acids bearing a second acidic functional group elsewhere in the molecule have received considerable attention as potential agonists or antagonists for excitatory amino acid neurotransmission (Johnson & Koerner, 1988; Watkins, Krogsgaard-Larsen & Honore, 1990). The synthesis of conformationally rigid analogues and homologues of the neurotransmitters glutamic and aspartic acids has aroused particular interest (Hashimoto, Ohfuné & Shirahama, 1995; Tanaka, Iwabuchi & Sawanishi, 1995; Ornstein *et al.*, 1993). For these reasons, we have recently focused our attention on new cyclic aspartate analogues in which the functional groups are situated on a rigid molecular framework. In a recent paper, we reported that the easily accessible compound (Z)-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-ylmethylidene]-2-phenyl-5(4*H*)-oxazolone readily gives, by reaction with cyclopentadiene, the corresponding 'exo'/'endo' Diels–Alder adducts with high 'exo' preference (Buñuel, Cativiela & Díaz-de-Villegas, 1994; Buñuel, Cativiela, Díaz-de-Villegas & García, 1994). These compounds can be easily isolated in diastereomerically pure form and provide useful key intermediates in the synthesis of two new conformationally constrained aspartic acid analogues with a norbornane skeleton: *exo*-(I) and *endo*-(I) (Buñuel, Cativiela & Díaz-de-Villegas, 1996).

In a previous paper, we described the crystal and molecular structure of the major product *exo*-(I) (Buñuel, Cativiela, Díaz-de-Villegas & Gálvez, 1996); the results of the single-crystal X-ray analysis on the minor diastereomer *endo*-(I) are reported here.



Comparison of the bond distances and angles in compound *endo*-(I) with those determined for other norbornane structures, and in particular with the compound *exo*-(I), reveals no strikingly unusual features and these parameters lie within the expected ranges.

The norbornyl rings of compounds *endo*-(I) and *exo*-(I) show distortion from the C_{2v} symmetry of the parent hydrocarbon although this distortion is more important in the previously reported compound, *exo*-(I). Both diastereomers show a synchro twist *S*-(+,+) (Altona & Sundaralingam, 1970). The twisting in amino acid derivative *endo*-(I) can be seen from the C1—C2—C3—C4 and C4—C5—C6—C1 dihedral angles of 3.8 (6) and 0.2 (8)°, respectively.

The main differences between aspartic acid analogues *exo*-(I) and *endo*-(I) involve the spatial arrangement of the methyl ester, benzamido and carboxylic acid groups