Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

(–)-(5*S*,8*S*,9*R*,10*S*,13*R*,14*R*)-15,16-Dideoxy-16,17-epoxy-16-oxospongian-15-yl acetate

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Received 13 February 2006
Accepted 20 February 2006
Online 18 March 2006

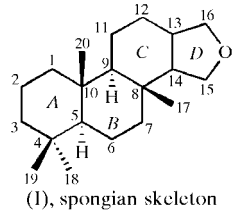
The title compound (aplyroseol-14), $C_{22}H_{34}O_4$, exhibits a lactone-based structure that is novel for spongian-type diterpenoids. The structure, which features a six-membered lactone ring, was proposed by Arnó, González & Zaragozá [*J. Org. Chem.* (2003), **68**, 1242–1251] on the basis of spectroscopic data and chemical correlations. This assignment has been confirmed, and it is shown that the molecule contains a *trans–anti–trans* 6/6/6 tricyclic hydrocarbon system and that the acetoxymethyl group lies in an equatorial position. Pairs of near-linear C—H···O interactions link molecules into extended chains.

Comment

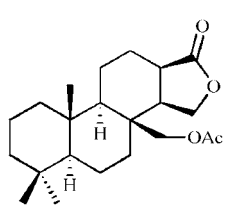
Spongian diterpenoids are bioactive natural products isolated exclusively from sponges and shell-less molluscs (nudibranchs), which are believed to be capable of sequestering the spongian-derived metabolites from the sponges on which they feed. Most of these compounds play a key role as eco-physiological mediators and are of interest as potential therapeutic agents (Arnó, Betancur-Galvis *et al.*, 2003).

The carbon skeleton (I), named 'spongian' in accordance with IUPAC recommendations (Kazlauskas *et al.*, 1979), was chosen as the fundamental parent structure for this family of natural compounds, with the numbering depicted. Thus, spongians typically exhibit the hydrocarbon ring system (I), consisting of a steroid-like *ABCD* ring system containing an oxygenated group, such as a tetrahydrofuran ring, and with varying oxidation patterns on rings *A*–*D*.

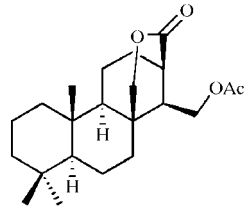
The title compound, (1*b*), was isolated from the sponge *Aplysilla rosea* Barrois by Taylor & Toth (1997), and the structure (1*a*), in which ring *D* is usually a five-membered lactone typical of other members of the spongian family (Cimino *et al.*, 1974; Karuso & Taylor, 1986; Miyamoto *et al.*, 1996), was assigned from one- and two-dimensional ^{1}H NMR data, high-resolution mass spectrometry, and IR spectroscopy. Following our studies directed towards the synthesis of C-17-functionalized spongians (Arnó *et al.*, 2001), we selected (1*a*) as a potential target compound and we readily synthesized



(I), spongian skeleton



(1*a*)



(1*b*)

a compound (Arnó, González & Zaragozá, 2003) whose spectroscopic data were in apparently good agreement with those reported for natural aplyroseol-14. However, a careful study of the spectroscopic data, in particular the IR and NMR spectra, indicated that the molecule contained the six-membered lactone (1*b*) instead of the expected five-membered one seen, for example, in (5*R**,7*S**,8*S**,9*S**,-10*R**,13*S**,14*S**)-16-oxospongian-7,17-diyl diacetate (Karuso & Taylor, 1986) or 7α-hydroxyspongian-16-one (Miyamoto *et al.*, 1996). We supported our assignment by synthesizing the proposed structure (1*a*) for aplyroseol-14 and making comparisons with the published data. As expected, the synthetic compound (1*a*) gave spectroscopic data that, although generally similar to those reported for natural (1*b*),

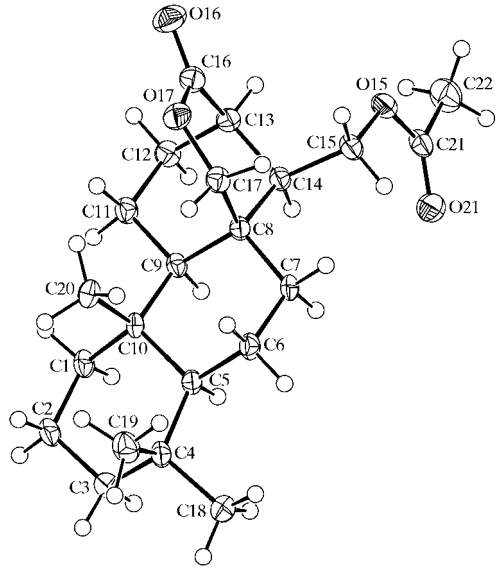


Figure 1
A view of (1*b*), showing the atom-numbering scheme and displacement ellipsoids at the 50% probability level.

  DOI: 10.1107/S0108270106006366

were nevertheless clearly different. Owing to the uniqueness of the carbon skeleton of (1*b*), together with apparent disagreement in some reported data (IR bands), a single-crystal X-ray study was carried out on synthetic (1*b*) in order to confirm the structural assignment. The ^{1}H NMR spectra of synthetic (1*b*) and natural (1*b*) were found to be in excellent agreement.

A perspective view of the molecule is shown in Fig. 1. Both the chemical connectivity and the relative stereochemistry are in full agreement with those proposed by Arnó, González & Zaragozá (2003) for aplyroseol-14 (1*b*). The stereochemistry at atoms C5 (*S*), C9 (*R*) and C10 (*S*) is invariant during the synthesis, but three new asymmetric centres were introduced at C8 (*S*), C13 (*R*) and C14 (*R*). The molecule contains a *trans–anti–trans* 6/6/6 tricyclic hydrocarbon system to which a six-membered lactone ring is attached at atoms C8 and C13. All six-membered rings adopt chair conformations with axially disposed methyl or lactone substituents. However, the lactone ring (C8/C14/C13/C16/O17/C17) is distorted towards a half-chair conformation; while atom C8 lies 0.734 (3) Å below the least-squares mean plane through atoms C14, C13, O17 and C17, atom C16 lies only 0.329 (3) Å above it. The acetoxymethyl group at atom C14 lies in an equatorial position. Bond lengths and angles are typical for such sterically non-strained molecules.

Molecules are linked by almost linear pairwise C—H···O interactions (Table 1 and Fig. 2). One of these interactions occurs between carbonyl atom O21 of the acetoxy group and atom H15 of the methylene group adjacent to the acetoxy group in a neighbouring molecule; the other involves methine atom H14 and lactone atom O17 in the same neighbouring molecule. The interactions link the molecules into chains running along the *b* axis. The C—H···O interactions contrast with the situation in analogous compounds containing hydroxy groups (Schmitz *et al.*, 1985; Karuso *et al.*, 1986; Miyamoto *et al.*, 1996), where the presence of the hydroxy groups leads to O—H···O=C hydrogen bonds being the primary intermolecular contacts.

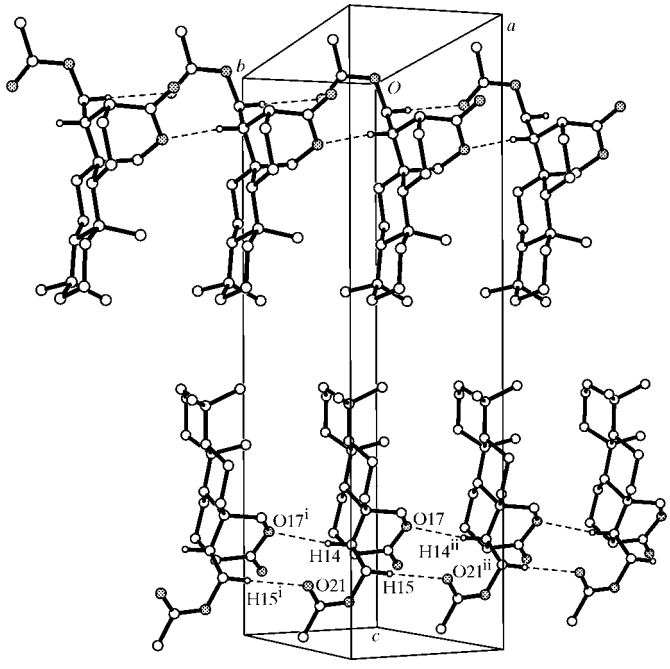
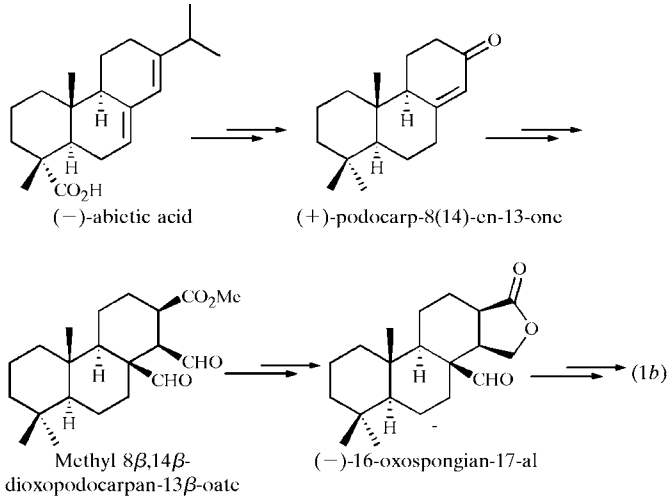


Figure 2
A view of the chains of molecules linked along the *b* axis by pairwise near-linear C—H···O interactions. C atoms are shown as large open circles, O atoms as dotted circles and H atoms as small open circles. [Symmetry codes: (i) $x, y+1, z$; (ii) $x, y-1, z$.]

Experimental

Compound (1*b*) was synthesized from the chiral synthon (+)-podocarp-8(14)-en-13-one, readily available from commercial (−)-abietic acid (Abad *et al.*, 1985; see scheme below). The absolute stereochemistry at atoms C5, C9 and C10 was therefore fixed. During the synthesis, the key intermediate methyl 8β,14β-dioxopodocarpan-13β-oate was prepared, in which three new stereocentres, *viz.* C8, C13 and C14, were introduced. This intermediate was transformed into (−)-16-oxospongian-17-al, confirming the absolute stereochemistry of all asymmetric centres. Finally, the latter was converted into (1*b*) by standard reduction followed by acetylation. This two-step process involved a translactonization reaction that occurred during the reduction step. Crystals were grown from a solution of (1*b*) in dichloromethane/hexane (1:4).



Crystal data

$C_{22}H_{34}O_4$
M_r = 362.49
Monoclinic, *C*2
a = 13.377 (2) Å
b = 6.0824 (8) Å
c = 23.834 (3) Å
β = 94.235 (2)°
V = 1933.9 (5) Å^3
Z = 4
D_x = 1.245 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3476 reflections
θ = 2.6–27.5°
μ = 0.08 mm^{-1}
T = 150 (2) K
Tablet, colourless
1.07 × 0.50 × 0.13 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
ω scans
5352 measured reflections
2382 independent reflections
2200 reflections with $I > 2\sigma(I)$
R_{int} = 0.133
θ_{max} = 27.5°
h = −17 → 15
k = −7 → 7
l = −30 → 22

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.049$	$w = 1/[\sigma^2(F_o^2) + (0.106P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.133$	$(\Delta/\sigma)_{max} = 0.001$
$S = 0.92$	$\Delta\rho_{max} = 0.40$ e Å^{-3}
2382 reflections	$\Delta\rho_{min} = -0.27$ e Å^{-3}
239 parameters	

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C14—H14···O17^{i}	1.00	2.49	3.486 (3)	171
C15—H15···O21^{ii}	0.99	2.52	3.509 (3)	173

Symmetry codes: (i) $x, y+1, z$; (ii) $x, y-1, z$.

The absolute configuration of (1*b*) was assigned as for (+)-podocarp-8(14)-en-13-one (Abad *et al.*, 1985), based on the absolute configuration of (−)-abietic acid as determined by optical rotatory dispersion measurements (*e.g.* Bose & Struck, 1959). All H atoms were included at geometrically calculated positions and constrained to ride on their parent C atoms at distances of 0.98, 0.99 or 1.00 Å for methyl, methylene or methine groups, respectively, and with U_{iso}(H) values of $1.5U_{eq}$(C) for methyl H atoms and $1.2U_{eq}$(C) for others. As there are no significant anomalous dispersion effects, Friedel opposites were merged prior to the final cycles of refinement.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT* and *SHELXTL* (Bruker, 2001); program(s) used to solve structure: *SIR2002* (Burla *et al.*, 2003); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003) and *SHELXTL*; software used to prepare material for publication: *enCIFer* (Allen *et al.*, 2004) and *PLATON*.

The authors thank the EPSRC (UK) for the funding of a diffractometer. We also gratefully acknowledge financial support by the Spanish Ministry of Education and Science under a 'Ramón y Cajal' research grant.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN3004). Services for accessing these data are described at the back of the journal.

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