organic compounds

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Crystal Structure
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The title compound (aplyroseol-14), C_{23}H_{34}O_6, exhibits a lactone-based structure that is novel for spongian-type diterpenes. The structure, which features a six-membered lactone ring, was proposed by Arnó, González & Zaragoza [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 mollusces (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, (1b), was isolated from the sponge Aplysilla rosea Barrois by Taylor & Toth (1997), and the structure (1a), 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 1H 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 (1a) as a potential target compound and we readily synthesized a compound (Arnó, González & Zaragoza, 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 (1b) instead of the expected five-membered one, for example, in (5R*,7S*,9S*,9S*,10R*,13S*,14S*)-16-oxospongian-7,17-diyldiacetate (Karus & Taylor, 1986) or 7α-hydroxyspongian-16-one (Miyamoto et al., 1996). We supported our assignment by synthesizing the proposed structure (1a) for aplyroseol-14 and making comparisons with the published data. As expected, the synthetic compound (1a) gave spectroscopic data that, although generally similar to those reported for natural (1b),

Figure 1

A view of (1b), showing the atom-numbering scheme and displacement ellipsoids at the 50% probability level.
were nevertheless clearly different. Owing to the uniqueness of the carbon skeleton of (1b), together with apparent disagreement in some reported data (IR bands), a single-crystal X-ray study was carried out on synthetic (1b) in order to confirm the structural assignment. The $^1$H NMR spectra of synthetic (1b) and natural (1b) 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 & Zaragóz (2003) for aplyrosol-14 (1b). 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 acetoxy-methyl 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.

**Experimental**

Compound (1b) was synthesized from the chiral synthon (+)-podo-carp-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-dioxopodocarp-13β-oate was prepared, in which these new stereocentres, viz. C8, C13 and C14, were introduced. This intermediate was transformed into (−)-16-oxospangion-17-al, confirming the absolute stereochemistry of all asymmetric centres. Finally, the latter was converted into (1b) by standard reduction followed by acetylation. This two-step process involved a transactonization reaction that occurred during the reduction step. Crystals were grown from a solution of (1b) in dichloromethane/hexane (1:4).

![Figure 2](image)

**Crystal data**

\[ \text{C}_{22}\text{H}_{30}\text{O}_{4} \]

\[ M_i = 362.49 \]

Monoclinic, C2

\[ a = 13.377 (2) \text{ Å} \]

\[ b = 6.0824 (5) \text{ Å} \]

\[ c = 23.834 (3) \text{ Å} \]

\[ β = 94.235 (2)° \]

\[ V = 1933.9 (5) \text{ Å}^3 \]

\[ Z = 4 \]

\[ D_{\text{cal}} = 1.245 \text{ Mg m}^{-3} \]

Mo Kα radiation

Cell parameters from 3476 reflections

\[ θ = 2.6–27.5° \]

\[ μ = 0.08 \text{ mm}^{-1} \]

\[ T = 150 (2) \text{ K} \]

Tablet, colourless

\[ 1.07 \times 0.50 \times 0.13 \text{ mm} \]

**Data collection**

Bruker SMART APEX CCD area-detector diffractometer

\[ 5352 \text{ measured reflections} \]

\[ 352 \text{ independent reflections} \]

\[ 2200 \text{ reflections with } I > 2σ(I) \]

**References**

Blake et al. · C22H30O4
organic compounds

Refinement

Refinement on $F^2$

$R(F^2 > 2\sigma(F^2)) = 0.049$

$wR(F^2) = 0.133$

$S = 0.92$

2382 reflections

239 parameters

H-atom parameters constrained

$w = 1/[\sigma^2(F^2) + (0.106P)^2]$

where $P = (F^2 + 2F'F)/3$

$\Delta\rho_{\text{max}} = 0.40$ e Å$^{-3}$

$\Delta\rho_{\text{min}} = -0.27$ e Å$^{-3}$

Table 1

Hydrogen-bond geometry (Å, °).

<table>
<thead>
<tr>
<th></th>
<th>D—H—A</th>
<th>D—H</th>
<th>H···A</th>
<th>D···A</th>
<th>D—H···A</th>
</tr>
</thead>
<tbody>
<tr>
<td>C14—H14—O17</td>
<td>1.00</td>
<td>2.49</td>
<td>3.486 (3)</td>
<td>171</td>
<td></td>
</tr>
<tr>
<td>C15—H15—O21</td>
<td>0.99</td>
<td>2.52</td>
<td>3.509 (3)</td>
<td>173</td>
<td></td>
</tr>
</tbody>
</table>

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

The absolute configuration of (1b) was assigned as for (+)-podo-carp-8(14)-en-13-one (Abad et al., 1985), based on the absolute configuration of (−)-acetic 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 $U_{eq}(H)$ values of 1.5$U_{eq}(C)$ for methyl H atoms and 1.2$U_{eq}(C)$ 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.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN0304). Services for accessing these data are described at the back of the journal.

References


