

H atoms treated by a mixture of independent and constrained refinement

Extinction correction: none  
Scattering factors from *International Tables for Crystallography* (Vol. C)

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Siemens (1995). *SMART and SAINT. Area-Detector Control and Integration Software*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Table 1. Selected geometric parameters (Å, °)

S1—O2	1.4236 (14)	O3—C14	1.206 (3)
S1—O1	1.4316 (14)	N1—C8	1.415 (2)
S1—N1	1.6353 (16)	C13—C14	1.466 (3)
S1—C5	1.7596 (17)		
O2—S1—O1	119.51 (9)	O1—S1—C5	108.34 (8)
O2—S1—N1	109.33 (9)	N1—S1—C5	106.64 (8)
O1—S1—N1	104.13 (9)	C8—N1—S1	125.03 (13)
O2—S1—C5	108.18 (9)	O3—C14—C13	126.8 (2)
C5—S1—N1—C8	59.9 (2)		

Table 2. Hydrogen-bonding geometry (Å, °)

D—H...A	D—H	H...A	D...A	D—H...A
N1—H1A...O3	0.88 (2)	1.97 (2)	2.708 (2)	141 (2)

The positions of all H atoms were calculated geometrically and a riding model was used in their refinement, except for H1A which was involved in the intramolecular hydrogen bond and was found in a residual electronic density map and refined freely.

Data collection: *SMART* (Siemens, 1995). Cell refinement: *SMART*. Data reduction: *SAINT* (Siemens, 1995). Program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997a). Molecular graphics: *SHELXTL* (Sheldrick, 1997b). Software used to prepare material for publication: *SHELXTL*.

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## ent-Isocopal-12-ene-15,16-dialdehyde from *Spongia officinalis*

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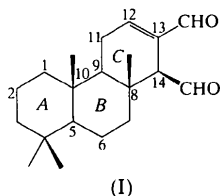
## Abstract

The X-ray analysis of the natural product *ent*-isocopal-12-ene-15,16-dialdehyde, 1,4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydro-4b,8,8,10a-tetramethyl-1,2-phenanthrene-dicarboxaldehyde, C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>, is reported. The compound was isolated, together with other diterpenes of the spongian type, from the diethyl ether soluble fraction of *Spongia officinalis* [Cimino, Morrone & Sodano (1982). *Tetrahedron Lett.* **23**, 4139–4142] and characterized. In the asymmetric unit, there are two molecules showing high geometrical and conformational similarity. The C-20 diterpenoid presents a *trans*-fused tricyclic system with a 1,4-dialdehyde function, adjacent to the double bond of the cyclohexene ring. Short intramolecular contacts, especially between the axial and isooriented methyl groups, cause significant distortions in the ring skeleton similar to that observed in other correlated structures. The profile of the molecule is rather bent (radius of curvature about 13 Å) in the direction perpendicular to the averaged molecular plane. Similar bending has been observed in the correlated scalaradial and 12-deacetoxy-scalaradial structures and helps to improve the intramolecular interactions.

† Associated to the National Institute for the Chemistry of Biological Systems (CNR).

### Comment

Among marine metabolites, terpenoid dialdehydes receive much attention for their biological activity often related to defence strategies (Faulkner, 1998, and previous reports). As a consequence, these substances are endowed with a wide pharmacological potential. The crystal structure determination of the title compound, (I), first studied by Cimino *et al.* (1982), is part of the research in progress concerning structural elucidations and biological properties of natural compounds (Puliti *et al.*, 1992, 1995; De Rosa *et al.*, 1994, 1995; Ciavatta *et al.*, 1997; Puliti & Mattia, 1999). In particular, the structure–activity relationship is important in the unsaturated 1,4-dialdehydes (polygodial type) because a few studies have focused on the specific relation between the stereochemistry of the aldehyde groups and biological activity, antifeedant and hot-tasting effects, especially (Cimino, Sodano & Spinella, 1987, and references therein).



In the asymmetric unit there are two molecules which display high geometrical and conformational similarity. The independent molecules are related by a rotation of about 40° around a non-crystallographic axis passing through the C3—C4 and C13—C14 bonds. On the best superimposition, the r.m.s. deviation of the corresponding atoms in the two molecules is 0.054 Å, the largest difference (0.171 Å) being associated with the carbonyl O1 atoms.

A perspective view of one molecule of *ent*-isocopal-12-ene-15,16-dialdehyde, (I), is given in Fig 1. The enantiomer was chosen according to the absolute stereochemistry of the scalarane skeleton (Kazlauskas *et al.*, 1980; Cimino, De Rosa *et al.*, 1987). On this basis the relative configurations at the chiral centres are fixed as 5*S*\*, 8*R*\*, 9*R*\*, 10*S*\*, 14*S*\*. The correct choice of the enantiomer is supported by the refined Rogers (1981) parameter. The C-20 diterpenoid presents a *trans* fused tricyclic system with four methyl substituents, three of which are axially  $\beta$ -oriented at the C4, C8 and C10 atoms, respectively. Moreover, two vicinal aldehyde functions are present in the C ring, adjacent to the intraring C12—C13 double bond, the one at C14 is in the equatorial  $\beta$ -orientation. The stereochemistry of the aldehyde groups was proved to be specifically related to the biological activity often shown by this class of compounds. In fact, the distance between carbonyl groups, depending on the orientation of the CHO substituent at the saturated C14 atom, is selective for the ability to form a covalent bond with receptors

(Cimino, Sodano & Spinella, 1987). Another restrictive factor for the biological activity of these molecules is the presence, in the nearby C7 position, of a bulky substituent that can hinder the surface complementarity between metabolite and receptor (De Rosa *et al.*, 1994; Puliti *et al.*, 1995).

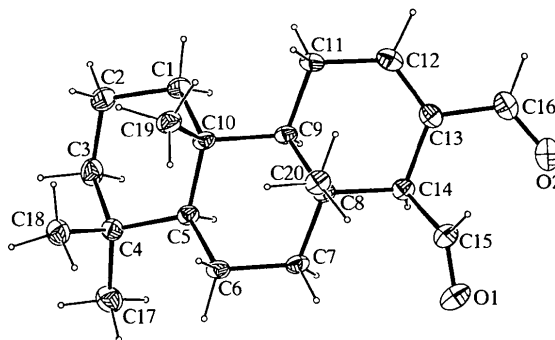


Fig. 1. Perspective view of one of the independent molecules of (I) with the atomic labelling for non-H atoms. Displacement ellipsoids are drawn at the 30% probability level.

The intramolecular geometry agrees well with the values observed in similar structures and, on average, the deviations of the corresponding values in the two molecules are within the experimental errors. In both molecules the C12—C13 bond distances 1.332 (5) and 1.338 (5) Å are typical of a localized double bond. The presence of axial and isooriented methyl groups gives rise to distortions in the geometry of the tricyclic skeleton similar to those observed in other correlated structures (Croft *et al.*, 1983; Cimino, De Rosa *et al.*, 1987; De Rosa *et al.*, 1994; Puliti *et al.*, 1995; Cambie *et al.*, 1999). In particular, the longest bond distances occur in the molecular backbone marked by the atoms C4, C5, C10, C9 and C8. The lengthening of these bonds, as well as the widening of some bond angles (see in Table 1 the values of C5—C4—C18, C4—C5—C10, C9—C8—C20 and C8—C9—C10) help to weaken the steric hindrances between the bulky substituents. In both independent molecules the conformations of A and B saturated rings are close to an ideal chair. Cyclohexene rings (C) adopt half-chair conformations with the atomic displacements C8A = 0.431 (3), C9A = 0.385 (3) and C8B = 0.452 (3), C9B = 0.379 (3) Å on the opposite side with respect to the best planes through the remaining ring atoms. Puckering parameters (Cremer & Pople, 1975) are:  $Q = 0.532$  (3) Å,  $\varphi = 28.2$  (4)°,  $\theta = 50.9$  (2)° in the A molecule and  $Q = 0.544$  (3) Å,  $\varphi = 27.1$  (4)°,  $\theta = 51.5$  (3)° in the B molecule. Deviations from ideal HC symmetries can also be described by the asymmetry parameters (Duax *et al.*, 1976)  $\Delta C_2(C8A—C9A) = 1.4$  (3)° and  $\Delta C_2(C8B—C9B) = 2.1$  (3)°. Conformational details for each ring are reported in the supplementary material. The carbonyl bond C16—O2 is *trans* with respect to the conjugated double bond: O2A—C16A—C13A—

C12A = -178.1 (3)°, O2B—C16B—C13B—C12B = -177.1 (4)°. The conformation of the other aldehyde group can be described by the torsion angle with respect to the C8—C14 bond that is 86.2 (4)° in the *A* molecule and 94.4 (4)° in *B*. This orientation is strongly controlled by the critical intramolecular interactions [O1A···C7A = 3.173 (4), O1A···O2A = 3.383 (4) and O1B···C7B = 3.249 (4), O1B···O2B = 3.309 (4) Å] and, in part, by packing requirements.

To gain more information about the limited rotational freedom around the C14—C15 bond, an energy minimization was carried on as a function of the torsion angle  $\theta$  (O1—C15—C14—C8) using *MM2* force field (Allinger, 1977, and subsequent versions). As starting molecule, the crystallographic model of (I) involving the *trans* conformation of the O2—C16—C13—C12 torsion angle was used. The trend of the calculated energies is shown in Fig. 2. The lowest energy minimum occurs at  $\theta = 90^\circ$  and corresponds to the conformation observed in the crystal. The only other favoured conformational region occurs in the  $\theta$  range from -100 to -20° with small differences in the relative energies:  $\Delta E$  from 3.6 to 5.1 kJ mol<sup>-1</sup>.

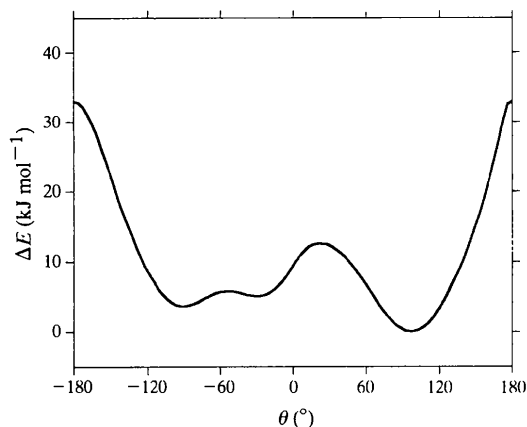


Fig. 2. Potential-energy curve of (I) calculated as a function of the torsion angle O1—C15—C14—C8.

As shown in Fig. 3 the molecule presents a remarkable bend approximately perpendicular to the best molecular plane. The bending can be evaluated by the dihedral angle between the average planes through the *A* and *C* rings that is 32° in both the independent molecules. It corresponds to a radius of curvature close to 13 Å. Similar bending has been observed in the correlated structures of 12-deacetoxy-scalarial (De Rosa *et al.*, 1994), scalarial (Puliti *et al.*, 1995), as well as of scalarolide and scalarin (Cambie *et al.*, 1999), and helps to improve intramolecular interactions.

The packing is governed by normal van der Waals interactions: carbon-carbon distances > 3.59 Å. The shortest intermolecular contacts involve the carbonyl-O atoms: O1B···C12B(*x* + 1, *y*, *z*) = 3.218 (4),

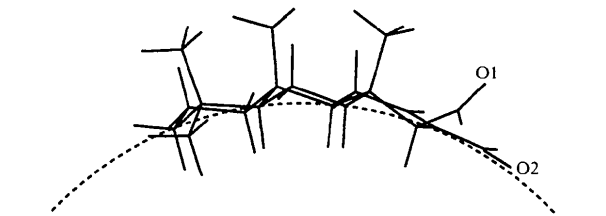


Fig. 3. View of the molecular bending approximately normal to the average molecular plane.

O1B···C11B(*x* + 1, *y*, *z*) = 3.264 (4), O2B···C16B( $\frac{1}{2}$  + *x*,  $\frac{1}{2}$  - *y*, 1 - *z*) = 3.435 (5), O1A···C12A(*x* + 1, *y*, *z*) = 3.453 (4), O1A···C9A( $\frac{1}{2}$  + *x*,  $\frac{3}{2}$  - *y*, 1 - *z*) = 3.482 (4) Å. They form, in addition to the above mentioned intramolecular interactions, further restrictions of the rotational-freedom of the C15—O1 aldehyde group.

## Experimental

Crystals of the title compound were obtained by slow evaporation of an ethanol-ethyl ether solution at room temperature.

### Crystal data

C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>  
*M<sub>r</sub>* = 302.46  
 Orthorhombic  
*P*2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>  
*a* = 7.3308 (12) Å  
*b* = 12.733 (3) Å  
*c* = 37.471 (7) Å  
*V* = 3497.7 (12) Å<sup>3</sup>  
*Z* = 8  
*D<sub>x</sub>* = 1.1487 Mg m<sup>-3</sup>  
*D<sub>m</sub>* not measured

Cu *K*α radiation  
 $\lambda$  = 1.54056 Å  
 Cell parameters from 25 reflections  
 $\theta$  = 25–30°  
 $\mu$  = 0.5548 mm<sup>-1</sup>  
*T* = 293 K  
 Prism  
 0.45 × 0.23 × 0.13 mm  
 Colourless

### Data collection

Enraf-Nonius CAD-4 diffractometer  
 $\omega$ - $\theta$  scans, as suggested by peak-shape analysis  
 Absorption correction: none  
 4101 measured reflections  
 4101 independent reflections  
 3186 reflections with *I* > 2 $\sigma$ (*I*)

$\theta_{\max}$  = 75°  
*h* = 0 → 9  
*k* = 0 → 15  
*l* = 0 → 47  
 4 standard reflections  
 frequency: 120 min  
 intensity decay: 3%

### Refinement

Refinement on *F*  
*R* = 0.044  
*wR* = 0.049  
*S* = 0.918  
 3186 reflections  
 399 parameters  
 H-atom parameters not refined  
 $w = 1/[\sigma^2(F_o) + (0.02F_o)^2 + 0.3]$  (Killean & Lawrence, 1969)  
 $(\Delta/\sigma)_{\max} = 0.0006$

$\Delta\rho_{\max} = 0.15 \text{ e } \text{Å}^{-3}$   
 $\Delta\rho_{\min} = -0.13 \text{ e } \text{Å}^{-3}$   
 Extinction correction: (Stout & Jensen, 1968)  
 Extinction coefficient:  $4.4(6) \times 10^{-7}$   
 Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)  
 Absolute structure: Rogers (1981)  
 Rogers parameter = 0.925 (6)

Table 1. Selected geometric parameters (Å, °)

O1A—C15A	1.197 (4)	O1B—C15B	1.214 (4)
O2A—C16A	1.225 (5)	O2B—C16B	1.204 (5)
C4A—C5A	1.555 (4)	C4B—C5B	1.553 (4)
C5A—C10A	1.549 (4)	C5B—C10B	1.564 (4)
C8A—C9A	1.564 (4)	C8B—C9B	1.546 (4)
C8A—C14A	1.567 (4)	C8B—C14B	1.569 (4)
C9A—C10A	1.576 (4)	C9B—C10B	1.570 (4)
C11A—C12A	1.488 (5)	C11B—C12B	1.473 (5)
C12A—C13A	1.332 (5)	C12B—C13B	1.338 (5)
C13A—C14A	1.514 (4)	C13B—C14B	1.515 (5)
C13A—C16A	1.454 (5)	C13B—C16B	1.452 (5)
C14A—C15A	1.519 (4)	C14B—C15B	1.508 (5)
C5A—C4A—C18A	114.8 (2)	C5B—C4B—C18B	114.1 (2)
C4A—C5A—C10A	117.0 (2)	C4B—C5B—C10B	116.8 (2)
C6A—C7A—C8A	113.9 (2)	C6B—C7B—C8B	113.1 (2)
C9A—C8A—C20A	113.5 (2)	C9B—C8B—C20B	113.6 (2)
C8A—C9A—C10A	115.7 (2)	C8B—C9B—C10B	117.3 (2)
C5A—C10A—C19A	114.1 (2)	C5B—C10B—C19B	113.8 (2)
C11A—C12A—C13A	124.1 (3)	C11B—C12B—C13B	124.5 (3)
C12A—C13A—C14A	122.6 (3)	C12B—C13B—C14B	122.2 (3)
O1A—C15A—C14A	124.3 (3)	O1B—C15B—C14B	122.8 (3)
O2A—C16A—C13A	122.8 (3)	O2B—C16B—C13B	124.3 (3)
C6A—C5A—C10A—C1A	174.9 (2)		
C7A—C8A—C9A—C11A	-179.9 (2)		
C14A—C8A—C9A—C11A	-63.8 (3)		
C16A—C13A—C14A—C15A	43.0 (4)		
C12A—C13A—C16A—O2A	-178.1 (3)		
C8A—C14A—C15A—O1A	86.2 (4)		
C6B—C5B—C10B—C1B	175.3 (2)		
C7B—C8B—C9B—C11B	178.8 (2)		
C14B—C8B—C9B—C11B	-65.3 (3)		
C16B—C13B—C14B—C15B	42.1 (4)		
C12B—C13B—C16B—O2B	-177.1 (4)		
C8B—C14B—C15B—O1B	94.4 (4)		

The structure was solved using the *SIR92* package (Altomare *et al.*, 1993). H atoms were placed on the basis of geometrical considerations and  $\Delta F$  map suggestions for methyl groups. All H atoms were included in the final refinement as fixed atoms with  $B_{\text{iso}}$  set equal to  $B_{\text{eq}}$  of the parent atom. The anomalous dispersion terms of O and C are small and not sufficient to determine unquestionably the absolute configuration. However, the refined Rogers parameter supports the correctness of the absolute configuration chosen according to that of the scalarane skeleton (Kazlauskas *et al.*, 1980; Cimino, De Rosa *et al.*, 1987). All calculations were performed using *SDP* software (Enraf–Nonius, 1985) on a MicroVAX 3100 computer.

The *MM2* energy minimization (Allinger, 1977) was performed on a Pentium 166 PC using the *HyperChem* 4.5 software (Hypercube, 1994). The potential-energy curve was computed by incrementing  $\theta$  in the 360° space in steps of 5°. The convergence criterium was set to an r.m.s. gradient less than 0.2 kJ mol<sup>-1</sup> Å<sup>-1</sup>. In order to constrain the  $\theta$  torsion angle, a high harmonic restoring force (4000 kJ mol<sup>-1</sup> degree<sup>-2</sup>) has been introduced at every step of the geometry optimization. The restoring force has been removed during the evaluation of the total energy.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: KA1332). Services for accessing these data are described at the back of the journal.

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## 2-(2-Fluoro-4-nitroanilinoethyl)benzaldehyde and N-(2-fluoro-4-nitrophenyl)-1-methoxy-1,2,3,4-tetrahydroisoquinoline

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## Abstract

2-(2-Fluoro-4-nitroanilinoethyl)benzaldehyde, C<sub>15</sub>H<sub>13</sub>FN<sub>2</sub>O<sub>3</sub>, exists as the aldehyde form with essentially

† Deceased.