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Ophiobolin A

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Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.007 Å
R factor = 0.054
wR factor = 0.114
Data-to-parameter ratio = 8.3

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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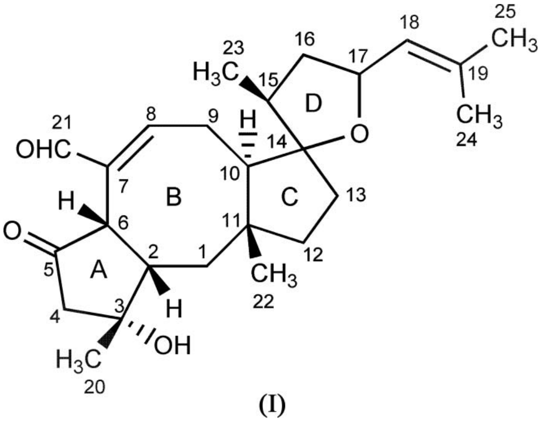
The title compound, namely (2′*S*,3′*S*,3a*R*,5′*R*,6a*S*,9*R*,9a*S*,10a*R*)-1,3a,4,4′,5′,6a,7,8,9,9a,10,10a-dodecahydro-9-hydroxy-3′,9,10a-trimethyl-5′-(2-methylpropen-1-yl)-7-oxospiro[dicyclopenta[*a*,*d*]cyclooctene-3(2*H*),2′(3′*H*)-furan]-6-carbaldehyde, $C_{25}H_{36}O_4$, displays phytotoxic behaviour that may be correlated with some structural features of the molecule. The eight-membered ring of the terpenoid tricyclic skeleton is *cis*- and *trans*-joined with the fused five-membered rings. One intramolecular O—H$\cdots$O hydrogen bond and two intermolecular C—H$\cdots$O hydrogen bonds are present.

Comment

Ophiobolin A was the first member of a group of polycyclic sesterterpenoids to be isolated and characterized (Ishibashi & Nakamura, 1958; Nozoe *et al.*, 1965). Structural studies were reported on its methoxybromide and tetrahydro derivatives (Morisaki *et al.*, 1968; Anastasia *et al.*, 1978). Ophiobolins have been extensively studied (Fujiwara *et al.*, 2000, Au *et al.*, 2000). Recently, it has been shown that the phytotoxic behaviour of ophiobolin A may be correlated to some structural features of the molecule, such as the presence of the hydroxy group at C3, the aldehyde group at C7 and the stereochemistry at C6 (Evidente *et al.*, 2006). Here, we report a low-temperature X-ray crystallographic analysis of ophiobolin A, (I), in order to contribute to a better understanding of the role of the stereochemistry of the carbotricyclic ring system in the affinity of the receptors.



(I)

The title compound (Fig. 1) shows the C25 terpenoid tricyclic skeleton of ophiobolins, consisting of fused five-, eight- and five-membered rings (rings *A*, *B* and *C*, respectively). A 2-isopropylidene-4-methyltetrahydrofuran side-chain is attached to ring *C* by the spiro-C atom at the 5-

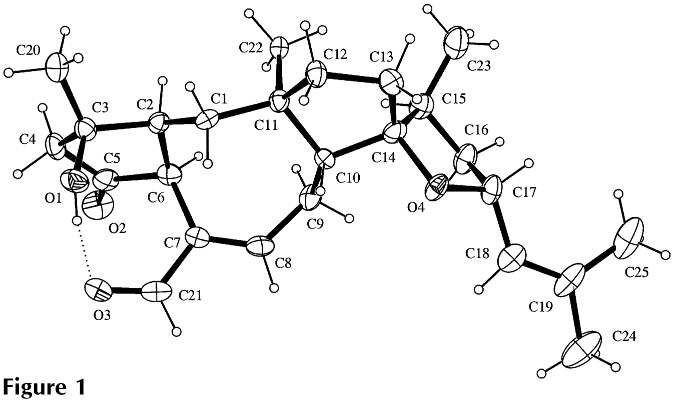


Figure 1
A view of the molecular structure of ophiobolin A. Displacement ellipsoids are drawn at the 50% probability level. The dashed line indicates the intramolecular hydrogen bond.

position of the tetrahydrofuran ring (ring *D*). The absolute configuration of the molecule has been assigned in accordance with the methoxybromide derivative (Morisaki *et al.*, 1968) as *S*, *R*, *S*, *R*, *R*, *S*, *S*, *R* at C2, C3, C6, C10, C11, C14, C15, C17, respectively. All bond lengths and angles (Table 1) are in normal ranges (Allen *et al.*, 1987); only a slight contraction of the C10—C11—C12 angle may be noted, probably as a consequence of the puckering of ring *C* and its junction with ring *B*. Rings *A* and *B* are *cis*-joined (H2—C2—C6—H6 = 31.3°), while rings *B* and *C* are *trans*-joined (C22—C11—C10—H10 = −179.7°). Both *A* and *C* rings adopt an envelope conformation, with atom C3 0.52 (6) Å out of the plane defined by atoms C2/C4/C5/C6 and atom C11 0.66 (5) Å out of the plane defined by atoms C10/C12/C13/C14.

The eight-membered ring *B* adopts a twist–boat conformation [atom C1 lies 0.39 (5) Å above and atom C11 lies 0.43 (5) Å below the plane defined by atoms C2/C6/C9/C10], which allows an intramolecular O—H···O hydrogen bond. Two additional C—H···O hydrogen bonds are present (Table 2), involving atoms C4 and C8. An envelope conformation is adopted by ring *D*, but, in contrast with the methoxybromide derivative, atom C17 atom is 0.50 (6) Å out of the plane through atoms O4/C14/C15/C16. In the isopropylidene side-chain, the mean plane of atoms C18/C19/C24/C25 including the C18═C19 double bond is tilted with respect to the mean plane of ring *D* by 63.5 (3)°. A *transoid* conformation of the H atoms bound to C17 and C18 is adopted (H17—C17—C18—H18 = 149.8°).

Experimental

Ophiobolin A was purified from the culture filtrate of *Dreschlera gigantea* (Biological Control of Weeds Collection at the Plant Pathology Department, University of Florida/IFAS, Gainesville, Florida, USA, No. LCLF-1), which was isolated during extensive field surveys in Florida from naturally infected large crabgrass (*Digitaria sanguinalis*). This fungus was grown as recently described by some of us (Evidente *et al.*, 2006). Its culture filtrates (2.7 l) were exhaustively extracted with EtOAc and the organic extract, showing a high phytotoxicity when assayed on detached leaves of *Phalaris canariensis*, was fractionated by column chromatography ($CHCl_3$–^{i}PrOH, 94:6 *v*/*v*) followed by preparative thin-layer chromatography. The residue of the third fraction (149.0 mg) was crystallized three times from ethyl acetate–*n*-hexane (1:5 *v*/*v*) to give the main metabolite (43 mg) as a white crystalline powder. Single crystals of (I) suitable for X-ray analysis were obtained by slow evaporation of a benzene solution.

Crystal data

$C_{25}H_{36}O_4$
$M_r = 400.54$
Orthorhombic, $P2_12_12_1$
$a = 7.251$ (4) Å
$b = 14.756$ (9) Å
$c = 20.55$ (2) Å
$V = 2199$ (3) Å^3
$Z = 4$
$D_x = 1.210$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.08$ mm^{-1}
$T = 173$ (2) K
Prism, colourless
0.20 × 0.20 × 0.07 mm

Data collection

Bruker Nonius KappaCCD area-detector diffractometer
Thick–slice φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker Nonius, 2002)
$T_{min} = 0.980$, $T_{max} = 0.994$
7226 measured reflections
2208 independent reflections
1356 reflections with $I > 2\sigma(I)$
$R_{int} = 0.112$
$\theta_{max} = 25.0°$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.054$
$wR(F^2) = 0.114$
$S = 1.03$
2208 reflections
267 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0367P)^2 + 0.6026P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.24$ e Å^{-3}
$\Delta\rho_{min} = -0.25$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C3	1.434 (5)	O4—C14	1.453 (5)
O2—C5	1.207 (6)	C2—C6	1.556 (6)
O3—C21	1.202 (6)	C10—C11	1.551 (6)
O4—C17	1.439 (6)	C18—C19	1.315 (7)
C4—C3—C2	102.3 (4)	C12—C11—C10	98.5 (4)
O2—C5—C6	124.7 (5)	C1—C11—C10	115.8 (4)
C4—C5—C6	109.3 (4)	O4—C14—C15	105.2 (4)
C7—C6—C5	114.2 (4)	O4—C17—C16	103.6 (4)
C21—C7—C6	120.9 (4)	C18—C17—C16	114.5 (4)
C9—C10—C11	119.3 (4)	C19—C18—C17	128.0 (6)
C14—C10—C11	105.6 (4)	O3—C21—C7	125.4 (5)
O1—C3—C4—C5	−90.6 (5)	C12—C13—C14—O4	−122.9 (4)
C3—C2—C6—C7	−96.6 (5)	O4—C17—C18—C19	−150.5 (5)
C3—C2—C6—C5	29.8 (4)	C16—C17—C18—C19	94.3 (6)
C14—C10—C11—C12	−44.5 (4)	C8—C7—C21—O3	171.4 (5)
C9—C10—C11—C1	66.0 (5)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O3	0.84	2.01	2.794 (5)	154
C4—H4*A*···O3^{i}	0.99	2.47	3.352 (6)	148
C8—H8···O2^{ii}	0.95	2.54	3.328 (6)	140

Symmetry codes: (i) $x + \frac{1}{2}, -y + \frac{3}{2}, -z + 1$; (ii) $x - 1, y, z$.

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All H atoms were positioned geometrically, except for the hydroxy H atom, which was found in a difference Fourier map. They were constrained to standard bond lengths (Csp^2-H = 0.95 Å, Csp^3-H = 0.98, 0.99 and 1.00 Å for methyl, methylene and methyne groups, respectively, and O—H = 0.84 Å) and allowed to ride on their parent atoms, with $U_{iso}(H) = U_{eq}(C,O)$. In the absence of any significant anomalous scattering, Friedel pairs were averaged prior to the final refinement and the absolute configuration was set by reference to the bromomethoxy derivative of ophiobolin A (Morisaki *et al.*, 1968). The poor quality of the crystal may explain the rather high value of R_{int}.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX/LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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