organic compounds

Two natural products from the algae *Laurencia scoparia*

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The structures and absolute stereochemistries of two chamigrene-type metabolites (spiro[5.5]undecane derivatives) isolated from the red algae *Laurencia scoparia* are described. One, a non-sesquiterpene named maílione (8-bromo-9-hydroxy-7,7-dimethyl-11-methylenespiro[5.5]undec-1-en-3-one), $C_{14}H_{19}BrO_2$, was detected previously in *Laurencia cartilaginea*, while the other, the sesquiterpene isorigidol (8-bromo-3,7,7-trimethyl-11-methylenespiro[5.5]-undec-1-ene-3,9-diol), $C_{15}H_{23}BrO_2$, is a new isomer of rigidol, first isolated from *Laurencia rigida*. The *A* rings of these spirocyclic compounds show the same carbon skeleton. However, the relative stereochemistry of the 8-Br and 9-OH substituents is different. While maílione displays the usual *syn* (or *cis*) relative stereochemistry of the bromohydroxy vicinal group, isorigidol shows an *anti* (or *trans*) arrangement. The 8-Br and 9-OH groups are both in equatorial positions in isorigidol, while the 9-OH group is axial in maílione, as in most chamigrenes. The absolute configurations of the chiral centers were determined as 6*S*, 8*S* and 9*R* in maílione, and 3*R*, 6*S*, 8*S* and 9*S* in isorigidol.

Comment

Chamigrenes are natural sesquiterpenes isolated from the red algae of the genus *Laurencia* and from sea hares (opistho branch mollusks of the genus *Aplysia*) which feed on it. They comprise a large group of bicyclic compounds with a spiro[5.5]undecane derivative carbon skeleton. The structures of two representative chamigrenes, isoobtusol, (I), and cartilagineol, (II) (González *et al.*, 1979; Francisco *et al.*, 1998), as well as the structure of obtusol acetate (Perales *et al.*, 1979), have been reported. The structures of other chamigrenes, such as rigidol, (III) (König & Wright, 1997), have been determined by spectroscopic measurement, but have not been established by X-ray diffraction. The structures of maílione, (IV), and

isorigidol, (V), described in this manuscript, are compared with the proposed stereochemistry of rigidol (König & Wright, 1997).
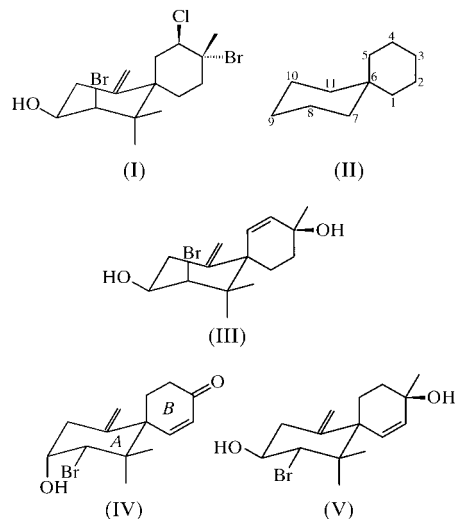
In accord with the literature, the six-membered rings of the spironic system are labelled *A* and *B*, as shown in the Scheme. Ring *A* (C6–C11) shows the same hydrocarbon skeleton and substitution pattern (8-bromo-3-hydroxy) in compounds (I)–(V). The second ring, *B* (C1–C6), has different substituents and can include a double bond. The most significant difference is the presence of a methyl group substituent at C3 in (I)–(III) and (V) (sesquiterpenes). This group is replaced by a carbonyl group in maílione (non-sesquiterpene). Compound (V) crystallizes with two molecules per asymmetric unit which are labelled (V*A*) and (V*B*). Molecular dimensions in (IV) and both molecules of (V) are as expected.

The results reported here establish unequivocally the absolute configurations of (IV) and (V), and especially the stereochemistry of the 8-bromo-9-hydroxy vicinal groups. While compounds (I)–(IV) display the usual *syn* (or *cis*) configuration (typical stereochemistry observed in chamigrenes), isorigidol, (V), shows an *anti* (or *trans*) arrangement. Only two other chamigrenes have been reported previously as having the hydroxy and bromine substituents in an *anti* configuration, namely (−)-10α-bromo-9β-hydroxy-α-chamigrene (König & Wright, 1997) and (1*Z*,8*R**,9*R**)-8-bromo-chamigra-1,11(12)-diene-9-ol (Wright & Coll, 1990). In maílione, (IV), the 8-bromo group is equatorial and the 9-hydroxy group is axial (8*S*, 9*R* configuration), and in isorigidol, (V), both substituents are equatorial (8*S*, 9*S* configuration). The expected configuration for this vicinal group in rigidol, (III) (König & Wright, 1997) (see Scheme), is 8*R*, 9*R*. While the absolute configuration of C6 is reversed in isorigidol and maílione from that in rigidol [*S* in (IV) and (V), and *R* in (III)], C3 adopts the same *R* configuration in rigidol and isorigidol, as expected.

Ring *A* in maílione and in both independent molecules of isorigidol (V*A* and V*B*) adopts a chair conformation, as can be seen in Figs. 1(*a*) and 1(*b*), and deduced from the Cremer & Pople parameters Q, θ and φ with values of 0.568 (7) Å, 7.8 (7)° and 41 (5)° in (IV), 0.584 (5) Å, 7.5 (5)° and 61 (4)° in

(VA), and 0.571 (5) Å, 8.6 (5)° and 81 (4)° in (VB) (Q = 0.6 Å and θ = 0 or 180° for the ideal cyclohexane chair). Ring B adopts an approximate half-chair puckering conformation. Q, θ and φ are 0.475 (7) Å, 127.0 (8)° and 48.2 (11)° in (IV), 0.511 (5) Å, 128.3 (6)° and 43.1 (7)° in (VA), and 0.511 (5) Å, 126.9 (6)° and 42.4 (7)° in (VB), while the expected θ and φ values for the exact half-chair conformation are 129.2 and 30°, respectively (Cremer & Pople, 1975). The conformations of both rings in the three independent molecules described here are for the most part very similar. Table 1 shows torsion angles where there are major differences between (IV) and (V). These differences arise because of the different relative stereochemistry of the bromohydroxy vicinal groups in ring A, as well as the different hybridization at C3 (sp^2 in maïlione and sp^3 in isorigidol).

The packing in both structures is determined by O—H···O hydrogen bonds; details are given in Tables 1 and 1. In maïlione, the 9-OH group is hydrogen bonded to the oxo group (O3) of a molecule r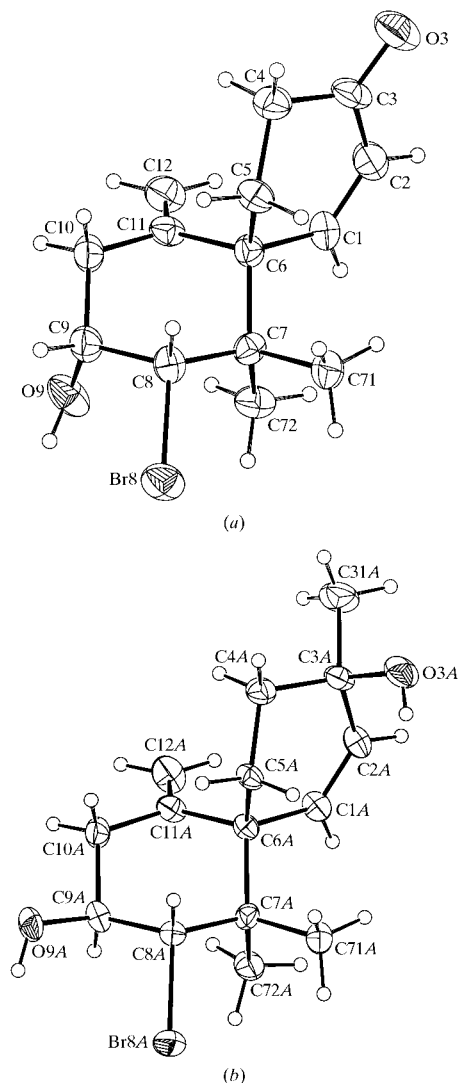elated by the twofold screw axis parallel to the b-axis direction and thereby forms an infinite spiral (see Table 2). In isorigidol, the formation of an $R_4^4(8)$ ring between four alternate (VA) and (VB) molecules is observed (Table 3). The ring corresponds to O9A—H9A···O9B—H9B···O3A^{iii}—H3A^{iii}···O3B^{iv}—H3B^{iv}···O9A [symmetry codes: (iii) $\frac{1}{2}$ + x, $\frac{3}{2}$ − y, 1 − z; (iv) $\frac{3}{2}$ − x, −y, $\frac{1}{2}$ + z]. Each of the molecules participates in two of these rings, thus forming a three-dimensional network.

Experimental

The air-dried algae were extracted three times with dichloromethane over a period of 1 d each time. Solvent was removed by evaporation at reduced pressure. The residue was fractioned on a silica-gel 60 flash chromatography column, with polarity-increasing mixtures of *n*-hex-ane–EtOAc–MeOH as eluent. Some fractions were further purified using a Sephadex LH-20 column with *n*-hexane–CHCl₃–MeOH (1:1:1). The crude compounds were purified by medium-pressure liquid chromatography on silica gel 100 with *n*-hexane–EtOAc mixtures to obtain pure compounds. Compounds (IV) and (V) were spectroscopically characterized before recrystallization. Single crystals of maïlione were obtained by slow evaporation of a mixture of *n*-hexane–CH₂Cl₂ at room temperature, while single crystals of isorigidol were obtained by slow evaporation of *n*-hexane at 268 (2) K.

Compound (IV)

Crystal data

$C_{14}H_{19}BrO_2$	Mo $K\alpha$ radiation
M_r = 299.20	Cell parameters from 24
Orthorhombic, $P2_12_12_1$	reflections
a = 9.9411 (16) Å	θ = 10.16–22.09°
b = 18.0364 (14) Å	μ = 3.097 mm⁻¹
c = 7.3758 (18) Å	T = 273 (2) K
V = 1322.5 (4) Å³	Prism, colourless
Z = 4	0.22 × 0.15 × 0.12 mm
D_x = 1.503 Mg m⁻³	

Data collection

Rigaku AFC-7S diffractometer	R_{int} = 0.042
$\theta/2\theta$ scans	θ_{max} = 27.49°
Absorption correction: ψ scan	h = −4 → 12
(North *et al.*, 1968; Molecular	k = −17 → 23
Structure Corporation, 1993)	l = −7 → 9
T_{min} = 0.549, T_{max} = 0.708	3 standard reflections
2172 measured reflections	every 150 reflections
2005 independent reflections	intensity decay: none
1106 reflections with $I > 2\sigma(I)$	

Refinement

Refinement on F^2	$(\Delta/\sigma)_{max} < 0.001$
$R[F^2 > 2\sigma(F^2)]$ = 0.044	$\Delta\rho_{max}$ = 0.70 e Å⁻³
$wR(F^2)$ = 0.128	$\Delta\rho_{min}$ = −0.74 e Å⁻³
S = 0.936	Extinction correction: $SHELXL$97
2005 reflections	Extinction coefficient: 0.0053 (14)
158 parameters	Absolute structure: Flack (1983)
H-atom parameters constrained	Flack parameter = −0.03 (2)
$w = 1/[\sigma^2(F_o^2) + (0.0766P)^2]$	
where $P = (F_o^2 + 2F_c^2)/3$	

Figure 1
The molecular structures of (*a*) maïlione and (*b*) one molecule of isorigidol, with displacement ellipsoids at the 30% probability level in each case. H atoms are represented by spheres of arbitrary radii.

Table 1
Hydrogen-bonding geometry (Å, °) for (IV).

D—H···A	D—H	H···A	D···A	D—H···A
O9—H9···O3^i	0.82	2.11	2.902 (7)	164

Symmetry code: (i) $\frac{1}{2}$ + x, $\frac{1}{2}$ − y, −z.

Table 2
Selected torsion angles (°) for molecules (IV), (VA) and (VB).

Molecule (IV) is maïlione, and molecules (VA) and (VB) are isorigidol.

	(IV)	(VA)	(VB)
Br8—C8—C9—O9	−62.2 (6)	61.9 (5)	61.7 (5)
C7—C8—C9—O9	65.6 (7)	−173.2 (4)	−174.1 (4)
O9—C9—C10—C11	−75.4 (8)	171.6 (4)	170.2 (4)
C1—C2—C3—O3	176.3 (6)	115.8 (6)	114.9 (5)
O3—C3—C4—C5	−146.7 (6)	−82.9 (5)	−82.0 (5)

Compound (V)

Crystal data

$C_{15}H_{23}BrO_2$
$M_r = 315.25$
Orthorhombic, $P2_12_12_1$
$a = 11.872$ (5) Å
$b = 11.897$ (4) Å
$c = 21.575$ (4) Å
$V = 3047.2$ (17) Å^3
$Z = 8$
$D_x = 1.374$ Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 25
reflections
$\theta = 7.53–11.40°$
$\mu = 2.691$ mm^{-1}
$T = 273$ (2) K
Parallelepiped, colourless
$0.23 \times 0.17 \times 0.13$ mm

Data collection

Rigaku AFC-7S diffractometer
$\theta/2\theta$ scans
Absorption correction: ψ scan
(North et al., 1968; Molecular
Structure Corporation, 1993)
$T_{min} = 0.577$, $T_{max} = 0.721$
4662 measured reflections
4525 independent reflections
2442 reflections with $I > 2\sigma(I)$

$R_{int} = 0.029$
$\theta_{max} = 27.50°$
$h = −1 \rightarrow 15$
$k = −1 \rightarrow 15$
$l = 0 \rightarrow 28$
3 standard reflections
every 150 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.094$
$S = 0.941$
4525 reflections
336 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0373P)^2]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.42$ e Å^{-3}
$\Delta\rho_{min} = −0.60$ e Å^{-3}
Extinction correction: SHELXL97
Extinction coefficient: 0.0032 (3)
Absolute structure: Flack (1983)
Flack parameter = −0.011 (11)

Table 3
Hydrogen-bonding geometry (Å, °) for (V).

D—H···A	D—H	H···A	D···A	D—H···A
O3A—H3A···O3B[i]	0.82	1.99	2.779 (6)	160
O3B—H3B···O9A[ii]	0.82	2.08	2.855 (5)	158
O9A—H9A···O9B	0.82	2.00	2.790 (5)	162
O9B—H9B···O3A[iii]	0.82	2.04	2.765 (5)	147

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

In both compounds, all H atoms were clearly visible in difference maps and these were then allowed for as riding atoms in the final refinement cycles, with O—H = 0.82 Å and C—H in the range 0.93–0.98 Å. In the refinement of (IV), there were 1765 unique reflections and 240 Friedel pairs; the corresponding numbers in the refinement of (V) were 3919 and 606, respectively. The values of the Flack parameters (see tabular material) establish unequivocally the absolute configurations of (IV) and (V).

For both compounds, data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1993); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *MSC/AFC Diffractometer Control Software*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ZORTEP* (Zsolnai & Pritzkow, 1995); software used to prepare material for publication: *PLATON*98 (Spek, 1990).

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