# 5. Rogiolenyne A, B, and C: the First Branched Marine $C_{15}$ Acetogenins. Isolation from the Red Seaweed *Laurencia microcladia* or the Sponge *Spongia zimocca* of Il Rogiolo

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It is shown here that the red seaweed *Laurencia microcladia*, collected off the torrent Il Rogiolo, south of Livorno, contains rogiolenyne A (= *(−)-(1R*,2S*,3R*,5S*,7S*)-2-(bromomethyl)-5-[(Z)-1-chlorohex-3-en-5-ynyl]-3-ethyl-4,8-dioxabicyclo[5.1.0]octane*; (−)-**1**) while the sponge *Spongia zimocca*, which grows in the same small area, contains rogiolenyne B (= *(−)-(2R*,3R*,4R*,5R*,7S*)-3-(bromomethyl)-5-chloro-7-[(Z)-1-chlorohex-3-en-5-ynyl]-2-ethyloxepan-4-ol*; (−)-**4a**) and its acetate, rogiolenyne C((−)-**4b**). These structures, which are based on extensive NMR and MS data and on chemical transformation, are the first examples of branched marine $C_{15}$ acetogenins. Biogenesis of (−)-**1** in *L. microcladia* is thought to involve C(12) extrusion form a $C_{15}$ linear tetraen-1-yne precursor *via* $H^+$-induced cyclopropane ring closure, followed by $Br^+$-induced cyclopropane ring opening, aided by $C-O^-$ attack (*Scheme 2*). It is also proposed that transfer of (−)-**1** to *S. zimocca* is followed by epoxide ring opening by $Cl^-$ to give (−)-**4a** and acetylation to give (−)-**4b**.

**Introduction.** – Seaweeds of the genus *Laurencia* and sea hares that feed on them are unique in containing acetogenins that are constituted of a halogenated *linear $C_{15}$ chain*; the chain may be either open or folded to form cyclic ethers or carbocycles, ending in an enyne or bromoallene function [1].

After over 25 years of continuous discoveries of structural variants on the above theme [1], we are here at a breakthrough with the first cases of marine acetogenins that are constituted of a *branched $C_{15}$ chain*; we have found them in the seaweed *Laurencia microcladia* and the sponge *Spongia zimocca* and, in order to avoid problems of taxonomy and origin[1]), we have given them the name rogiolenynes from the place of collection.

[1]) *L. microcladia* and *S. zimocca* grow in the same small area in front of the torrent Il Rogiolo, south of Livorno. We have already commented on the ecology of this sponge which proved to contain rogiolol acetate, the first $\beta$-chamigrane-type compound ever isolated from a sponge [3]; a red seaweed growing close to this sponge, then indicated as *Laurencia* sp. [3], has now been identified by Dr. *M. Verlaque* as *Laurencia microcladia* KÜTZNING, under the *caveat* that the genus *Laurencia* needs a complete revision. According to Dr. *Verlaque*, *L. microcladia* is a species characteristic of the tropical Atlantic [4], and our present collection, although not very typical, is similar to a sample previously collected in Corse [4]. A species with the name *L. microcladia* was recently collected at Cap Ferrat, Côte d'Azur, and found to contain eight-membered cyclic bromoallene ethers normally constructed on a linear $C_{15}$ chain [5]. So far, we have not identified any allene-bearing compound in our *L. microcladia*.

**Results and Discussion.** – NMR and HR-MS data (*Tables 1* and *2* and *Exper. Part*) show that rogiolenyne A ((–)-**1**[2]) from *L. microcladia* has the molecular formula $C_{15}H_{20}BrClO_2$ and the structure given in *Scheme 1*.

Table 1. *$^{13}$C-NMR Data* ($CDCl_3$) *for Rogiolenyne A* ((–)-**1**), *its Derivatives* (–)-**2** *and* (–)-**3**, *Rogiolenyne B* ((–)-**4a**), *and Rogiolenyne C* ((–)-**4b**)

| | (–)-**1** | (–)-**2** | (–)-**3** | (–)-**4a** | (–)-**4b**[b]) |
|---|---|---|---|---|---|
| C(1) | 82.58 (*d*) | 82.43 (*d*) | 83.49 (*d*) | 82.59 (*d*) | 82.64 (*d*) |
| C(2) | 79.80 (*s*) | [a]) | [a]) | 79.87 (*s*) | 79.80 (*s*) |
| C(3) | 110.88 (*d*) | 110.66 (*d*) | 108.48 (*d*) | 111.01 (*d*) | 111.12 (*d*) |
| C(4) | 140.79 (*d*) | 141.04 (*d*) | 141.19 (*d*) | 140.79 (*d*) | 140.63 (*d*) |
| C(5) | 34.33 (*t*) | 34.07 (*t*) | 128.04 (*d*) | 35.91 (*t*) | 36.07 (*t*) |
| C(6) | 63.42 (*d*) | 63.38 (*d*) | 137.76 (*d*) | 65.47 (*d*) | 65.63 (*d*) |
| C(7) | 73.72 (*d*) | 74.83 (*d*) | 72.85 (*d*) | 73.62 (*d*) | 73.33 (*d*) |
| C(8) | 30.73 (*t*) | 30.90 (*t*) | 33.63 (*t*) | 31.29 (*t*) | 31.70 (*t*) |
| C(9) | 53.17 (*d*) | 53.98 (*d*) | 54.43 (*d*) | 60.84 (*d*) | 57.23 (*d*) |
| C(10) | 55.93 (*d*) | 59.37 (*d*) | 59.13 (*d*) | 72.66 (*d*) | 72.45 (*d*) |
| C(11) | 46.82 (*d*) | [a]) | 144.90 (*s*) | 53.06 (*d*) | 50.81 (*d*) |
| C(12) | 74.82 (*d*) | 72.10 (*d*) | 71.85 (*d*) | 72.05 (*d*) | 72.72 (*d*) |
| C(13) | 23.45 (*t*) | 25.04 (*t*) | 25.44 (*t*) | 29.96 (*t*) | 27.05 (*t*) |
| C(14) | 11.05 (*q*) | 11.00 (*q*) | 10.77 (*q*) | 11.52 (*q*) | 11.45 (*q*) |
| C(15) | 30.47 (*t*) | 118.12 (*t*) | 117.13 (*t*) | 31.06 (*t*) | 30.14 (*t*) |

[a]) Not detected.

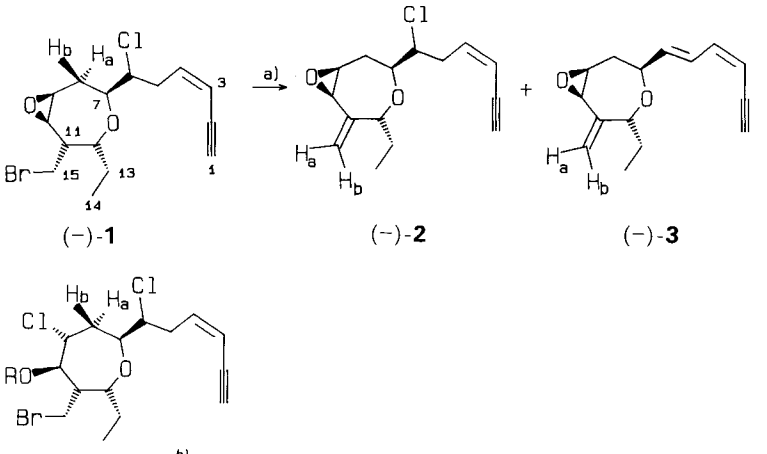
[b]) $CH_3CO$ 21.16 (*q*); $CH_3CO$ 168.99 (*s*).

Table 2. *$^1$H-NMR Data* ($CDCl_3$) *for Rogiolenyne A* ((–)-**1**)

| | |
|---|---|
| H–C(1) | 3.13 (*dd*, $J(1,3) = 2.3$, $J(1,4) = 0.9$) |
| H–C(3) | 5.59 (*ddt*, $J(3,4) = 10.9$, $J(3,1) = 2.3$, $J(3,5a) \approx J(3,5b) = 1.5$) |
| H–C(4) | 6.08 (*dtd*, $J(4,3) = 10.9$, $J(4,5a) \approx J(4,5b) = 7.3$, $J(4,1) = 0.9$) |
| 2 H–C(5) | 2.87 (*dddd*, $J_{gem} = 15.2$, $J(5a,4) = 7.3$, $J(5a,3) = 1.6$, $J(5a,6) = 4.5$) |
| | 2.69 (*dddd*, $J_{gem} = 15.2$, $J(5b,4) = 7.3$, $J(5b,3) = 1.5$, $J(5b,6) = 9.0$) |
| H–C(6) | 3.94 (*ddd*, $J(6,5a) = 4.5$, $J(6,5b) = 9.0$, $J(6,7) = 3.4$) |
| H–C(7) | 3.98 (*ddd*, $J(7,6) = 3.4$, $J(7,8a) = 1.5$, $J(7,8b) = 10.3$) |
| $H_a$–C(8) | 2.35 (*ddd*, $J_{gem} = 15.6$, $J(8a,7) = 10.5$, $J(8a,9) = 7.2$) |
| $H_b$–C(8) | 2.08 (*ddd*, $J_{gem} = 15.6$, $J(8b,7) = 10.3$, $J(8b,9) = 5.4$) |
| H–C(9) | 3.23 (*ddd*, $J(9,8a) = 5.4$, $J(9,8b) = 7.2$, $J(9,10) = 4.2$) |
| H–C(10) | 3.12 (*ddd*, $J(10,9) = 4.2$, $J(10,11) = 5.2$) |
| H–C(11) | 2.49 (*tdd*, $J(11,10) \approx J(11,15a) = 5.2$, $J(11,12) = 1.6$, $J(11,15b) = 9.3$) |
| H–C(12) | 3.73 (*ddd*, $J(12,11) = 1.6$, $J(12,13a) = 10.2$, $J(12,13b) = 4.2$) |
| 2 H–C(13) | 1.78 (*ddq*, $J_{gem} = 14.6$, $J(13a,12) = 10.2$, $J(13a,14) = 7.1$) |
| | 1.46 (*ddq*, $J_{gem} = 14.6$, $J(13b,12) = 4.2$, $J(13b,14) = 7.1$) |
| 3 H–C(14) | 0.98 (*t*, $J(14,13a) = J(14,13b) = 7.1$) |
| 2 H–C(15) | 3.58 (*dd*, $J(15a,11) = 5.4$, $J_{gem} = 10.6$) |
| | 3.38 (*dd*, $J(15b,11) = 9.3$, $J_{gem} = 10.6$) |

[2]) Systematic numbering is only used for retrieval purposes (see *Exper. Part* and abstract); all experimental data are discussed in terms of the numbering in structural formula (–)-**1**. No absolute-configuration meaning is implied by any of the structural formulae displayed here.

*Scheme 1*




*a*) 3% $K_2CO_3$/MeOH, r.t., 24 h.
*b*) 3% $K_2CO_3$/MeOH, r.t., 1 h.

The whole chain structure of (−)-**1** and the branching at C(11) find support in the $^1H,^1H$ COSY spectrum (*Fig. 1*); H–C(11) is coupled not only to H–C(10) and H–C(12) but also to the two diastereotopic protons at C(15) which are deshielded by the Br-atom ($\delta$(H) = 3.58 and 3.38 ppm) and coupled to the C-atom at 30.47 ppm (*t*). The Cl–C(6) group which is indicated by the MS fragment $[M - C_6H_6Cl]^+$ is part of the CH(6)(Cl)–CH(7)(O) portion, as indicated by the coupling ($^1J$) of *H*–C(6) and *H*–C(7) to the deshielded C-atoms at 63.42 and 73.72 ppm (*d*), respectively[3]. The *d*'s at 53.17 and 55.93 ppm for C(9) and C(10) are compatible with an epoxide group, while the *d* at 74.82 ppm indicates *O*-bridging at C(12). A *trans*-diaxial coupling of H–C(7) and $H_b$–C(8) supports the $\beta$-position for the chain at C(7), while a positive NOE for $H_b$–C(8)/H–C(12) indicates the $\alpha$-position for the Et group at C(12)[4]), and a small coupling between H–C(11) and H–C(12) supports the $\alpha$-position for the $CH_2Br$ group. Characteristic values for $J$(3,4) (10.9 Hz) and $\delta$(*H*–C(1)) (3.13 ppm) indicate the (*Z*)-configuration at C(3)=C(4).

The above conclusions are reinforced by the transformation of (−)-**1** in $K_2CO_3$/MeOH into a *ca.* 1:1 mixture of (−)-**2** and (−)-**3** (*Scheme 1*). The $CH_2$(15)Br $^1$H-NMR signals of (−)-**1** are replaced by the signals for an exocyclic methylidene group in (−)-**2** (*Exper. Part*). Moreover, formation of the dienyne system in (−)-**3** further supports the C(6) position for the Cl-atom in (−)-**1**.

The NMR spectra of rogiolenynes B ((−)-**4a**) and C ((−)-**4b**) from *S. zimocca* resemble much those for (−)-**1**, while the MS indicate an additional Cl-atom for both (−)-**4a** and (−)-**4b**, an OH group for (−)-**4a**, and an Ac group for (−)-**4b**; this fits a chlorohydrin and an acetylchlorohydrin group, respectively (*Table 1* and *Exper. Part*). At this point, the smooth change of (−)-**4b** into (−)-**1** on brief treatment with $K_2CO_3$/MeOH at r.t. (*Scheme*

[3]) For the alternative eight-membered cyclic structure with a $C_5$ linear side chain and Cl at C(7), the resonance of C(7) would be expected at higher field rather than that of C(6).

[4]) The signals of (−)-**1** of C(7) and C(12) of (−)-**11** appear *ca.* 5 ppm upfield when compared to oxepanes with *cis*-arrangement of the substituents at C(7) and C(12) [1][2]. These upfield shifts observed for (−)-**1** and all other rogiolenynes reported below must result from *γ-gauche* (1,3-diaxial) interactions.

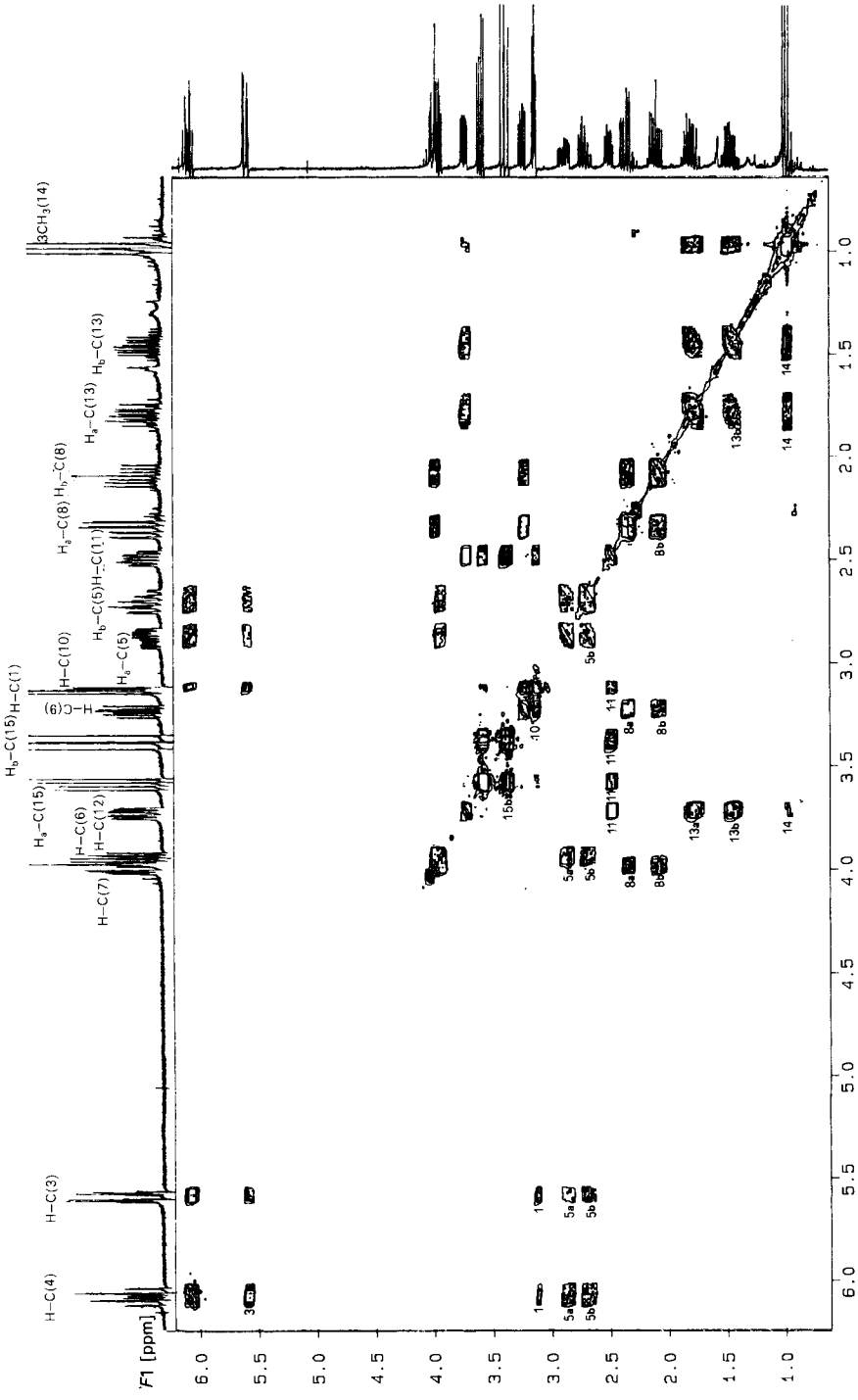



Fig. 1. *COSY 120° contour plot for rogiolenyne A* ((−)-**1**). Numbering at the contour maps refers to the ordinate scale.

*1*)[5]) only leaves the relative positions of the substituents within the chlorohydrin group to be established which is achieved by NMR data.

The position of the Cl-atom at C(9) in (–)-**4b** is indicated by the correlation of *H*–C(9) (defined by $^1H,^1H$ COSY) and *H*–C(10) with the C-atoms at 57.23 and 72.45 (*d*), respectively. Then, a W-coupling of H–C(11)/H–C(9) and H–C(10)/$H_a$–C(8) and small *J*'s for both H–C(9) and H–C(10) indicate that both H–C(9) and H–C(10) occupy pseudo-equatorial positions. This is confirmed by positive NOE's for $H_b$–C(8)/H–C(12) and

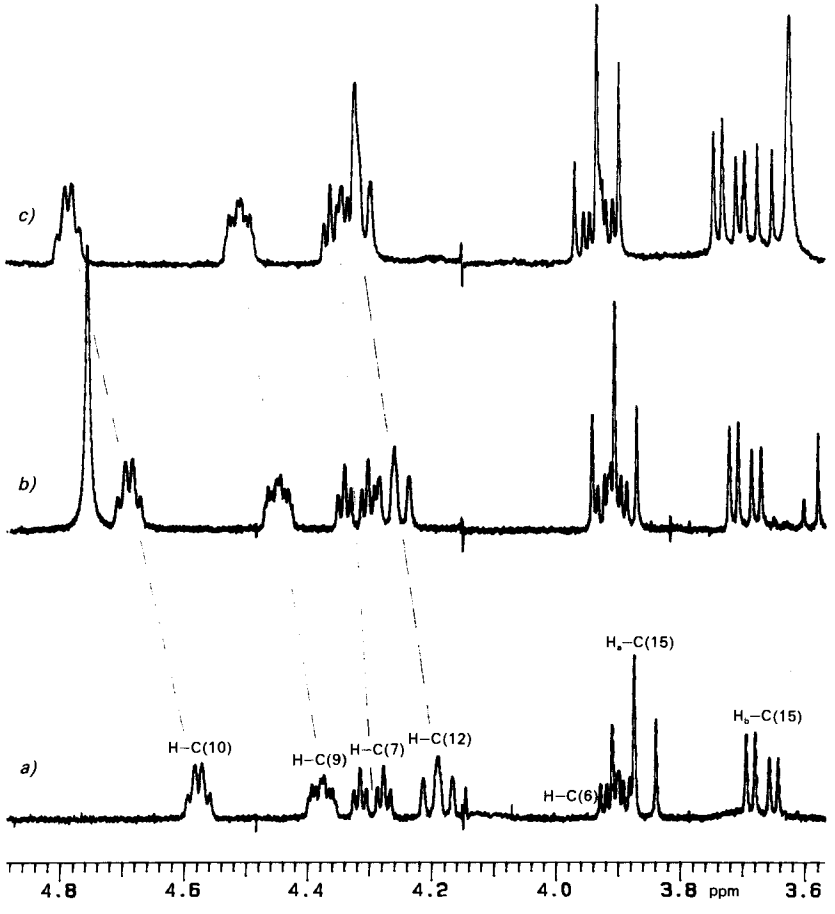


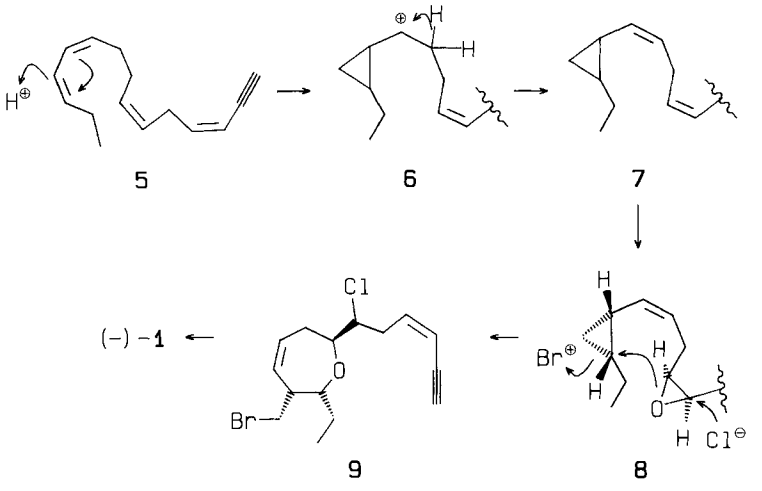

Fig. 2. *Downfield shifts with rogiolenyne B* ((–)-**4a**) *by Eu(fod)*$_3$. [Eu(fod)$_3$]/[(–)-**4a**] = 0 (*a*), 0.15 (*b*), 0.30 (*c*).

H–C(11)/H–C(12). Eu(fod)$_3$-induced deshielding of the H–C(12) resonance of (–)-**4a** (*Fig. 2*) establishes the *β*-position for the OH group (and therefore, also for the epoxide O-atom in (–)-**1**), while the quasi-insensitive resonance of H–C(7) further supports the *trans*-relationship between the side chains at C(7) and C(12).

The biogenesis of marine acetogenins constructed on a linear $C_{15}$ chain has always been postulated to start from $C_{15}$ linear polyen-1-yne precursors [1]; this has received some support from the isolation of structurally suitable precursors from some species of

[5]) Prolonged treatment leads to *β*-elimination of HBr from CH(11)–$CH_2$Br (→(–)-**1** + (–)-**2**; *Scheme 1*).

*Scheme 2*




*Laurencia* [1], although no biosynthetic experiment has ever been reported. For the above mentioned branched $C_{15}$ acetogenins, biogenesis from such a type of linear precursor can be imagined, too. An attractive hypothesis would involve $H^+$-catalyzed cyclopropane ring closure at C(11)–C(13) of the tetraen-1-yne precursor **5** to give trienyne **7** *via* cation **6** (*Scheme 2*). Epoxidation of **7** at C(6)=C(7) would give the key intermediate **8** which could undergo bromonium-ion (provided by haloperoxidase [6]) edge-insertion [7] into the cyclopropane ring concomitant with $Cl^-$ attack at C(6), epoxide opening, and ring closure at C(13) to give intermediate **9**; epoxidation of the latter would finally give rogiolenyne A ((–)-**1**).

As no trace of (–)-**1** was found in our *S. zimocca*, and neither (–)-**4a** nor (–)-**4b** was found in our *L. microcladia*[6]), it is conceivable that (–)-**1** is transferred from *L. microcladia* to *S. zimocca*[7]) where it undergoes epoxide opening by $Cl^-$ to give (–)-**4a** followed by acetylation to give (–)-**4b**. The rogiolenynes (–)-**4a** and (–)-**4b** are the first $C_{15}$ acetogenins ever found in a sponge; together with the $\beta$-chamigrene rogiolol acetate previously isolated from this collection of *S. zimocca* [3], they raise interesting problems of sponge/macrophyte interaction.

We thank Dr. *Marc Verlaque* (Université d'Aix-Marseille) for the identification of the alga and for stimulating comments, Mr. *L. Zuppiroli* for high-resolution mass spectra, and both MPI (Progetti di Interesse Nazionale) and CNR, Roma, for financial support.

[6]) In contrast, $C_{15}$ acetogenins with a linear chain, such as obtusin [8], proved to be common to both species.

[7]) Dr. *M. Verlaque*, who found no trace of macrophytes in our *S. zimocca*, suggested that transfer of metabolites from the alga to the sponge might occur *via* algal spores filtered by the sponge. Although this remains to be proved and, to the best of our knowledge, there is no precedence for such a mechanism, it is a fact that our *L. microcladia* was collected during its sporulation period (tetraspores).

## Experimental Part

1. *General.* See [3]. Moreover: HPLC: columns, 25 × 1 cm; solvent flux, 5 ml/min. NMR: $^1H,^1H$-coupling pattern by differential decoupling irradiations [9]; 90/120 $^1H,^1H$ COSY with (−)-**1**, (−)-**4a**, and (−)-**4b**; NOE means differential NOE; assignment of H-bearing C-atoms of (−)-**1** and (−)-**4b** from $^{13}C,^1H$-COSY [10]. HR-MS: *VG 70-70* spectrometer.

2. *Isolation. L. microcladia* (51 g dry weight), collected off the torrent Il Rogiolo (Livorno), was subjected to EtOH evaporation, hexane extraction (3 g of extract), and FC (hexane/$Et_2O$ gradient, 54 50-ml fractions). The residue from evaporation of *Fractions 11–18* (0.11 g) was subjected to reversed-phase HPLC (MeCN/$H_2O$ 65:35) to give *rogiolenyne A* ((−)-**1**; $t_R$ 6.5 min, 20 mg).

*S. zimocca* (90 g dry weight) was previously collected and worked up to isolate rogiolol acetate [3]; in the present work, fractions having the same polarity as those containing rogiolol acetate [3] were evaporated, and the residue was subjected to HPLC (hexane/$CH_2Cl_2$ 1:1, then hexane/(i-Pr)$_2$O 83:17) to give *rogiolenyne C* ((−)-**4b**; $t_R$ 19.0 min, 5.5 mg); fractions of higher polarity were evaporated, and the residue was subjected to HPLC (hexane/(i-Pr)$_2$O 4:1) to give *rogiolenyne B* ((−)-**4a**; 1.2 mg).

3. *Rogiolenyne A* (= *(−)-(1*R*,*2*S*,*3*R*,*5*S*,*7*S*)*-2-(Bromomethyl)-5-[(*Z*)*-1-chlorohex-3-en-5-ynyl]-3-ethyl-4,8-dioxabicyclo[5.1.0]octane*; (−)-**1**). Colorless oil. $[\alpha]_D = -22.8$ ($c = 0.18$, MeOH). UV (MeOH): 230 (sh, 12000), 221 (15900), 206 (sh, 3000). MS: 348, 346 (3, 2.5, $M^+$); 312, 310 (17, 17, $[M - HCl]^+$); 269, 267 (3, 7, $[M - Br]^+$); 235, 233 (24, 24, $[M - C_6H_6Cl]^+$). HR-MS: 310.0564 ($C_{15}H_{19}BrO_2$, calc. 310.0568).

4. *Treatment of (−)-***1** *with Base.* A suspension of (−)-**1** (0.006 g) in 3% $K_2CO_3$/MeOH (1 ml) was stirred at r.t. until disappearance of (−)-**1** (24 h). Then, sat. $NaHCO_3$ soln. was added and the mixture extracted twice with hexane. The org. phase was subjected to reverse-phase HPLC (MeCN/$H_2O$ 3:2): (−)-**2** ($t_R$ 11.0 min; 0.002 g, 42%) and (−)-**3** ($t_R$ 8.0 min; 0.002 g, 50%).

*15-Debromo-11,15-didehydrorogiolenyne A* ((−)-**2**). Colorless oil. $[\alpha]_D = -14.2$ ($c = 0.08$, $CHCl_3$). $^1H$-NMR ($CDCl_3$): 6.09 (*dtd*, $J(4,3) = 10.7$, $J(4,5a) \approx J(4,5b) = 7.3$, $J(4,1) = 0.9$, H–C(4)); 5.57 (*ddt*, $J(3,4) = 10.7$, $J(3,1) = 2,4$, $J(3,5a) \approx J(3,5b) = 1.5$, H–C(3)); 5.53 (br. *s*, $H_a$–C(15)); 5.36 (br. *s*, $H_b$–C(15)); 3.96 (*ddd*, $J(12,11) = 1.0$, $J(12,13a) = 8.2$, $J(12,13b) = 5.5$, H–C(12)); 3.88 (*m*, H–C(7)); 3.91 (*m*, H–C(6)); 3.59 (*d*, $J(10,9) = 4.4$, H–C(10)); 3.32 (*ddd*, $J(9,8b) = 3.2$, $J(9,8a) = 7.6$, $J(9,10) = 4.4$, H–C(9)); 3.13 (*dd*, $J(1,3) = 2.4$, $J(1.4) = 0.9$, H–C(1)); 2.88, 2.66 (2 *dddd*, $J_{gem} = 15.1$, $J(5a,4) = 7.3$, $J(5a,3) = 1.9$, $J(5a,6) = 4.3$ and $J_{gem} = 15.1$, $J(5b,4) = 7.2$, $J(5b,3) = 1.5$, $J(5b,6) = 10.7$, resp., 2 H–C(5)); 2.24 (*m*, 2 H–C(8)); 1.70 (*dq*, $J(13,12) = 5.5$, $J(13,14) = 7.3$, 2 H–C(13)); 0.98 (*t*, $J(14,13) = 7.3$, 3 H–C(14)).

*15-Debromo-6-dechloro-5,6,11,15-tetradehydrorogiolenyne A* ((−)-**3**). Colorless oil. $[\alpha]_D = -30.0$ ($c = 0.09$, $CHCl_3$). $^1H$-NMR ($CDCl_3$): 6.78 (*dddd*, $J(5,4) = 10.7$, $J(5,6) = 15.4$, $J(5,3) = 1.0$, $J(5,7) = 1.7$, H–C(5)); 6.47 (*tt*, $J(4,3) \approx J(4,5) = 10.7$, $J(4,1) \approx J(4,6) = 1.0$, H–C(4)); 5.42 (*ddt*, $J(3,4) = 10.7$, $J(3,1) = 2.5$, $J(3,5) \approx J(3,6) = 1.0$, H–C(3)); 5.96 (*ddt*, $J(6,5) = 15.4$, $J(6,7) = 6.1$, $J(6,4) \approx J(6,3) = 1.0$, H–C(6)); 5.47 (br. *s*, $H_a$–C(15)); 5.32 (*m*, $H_b$–C(15)); 4.39 (*ddd*, $J(7,6) = 6.1$, $J(7,8b) = 8.1$, $J(7,8a) = 1.8$, H–C(7)); 3.98 (*dt*, $J(12,13) = 6.6$, $J(12,15b) = 1.2$, H–C(12)); 3.61 (br. *d*, $J(10,9) = 4.3$, H–C(10)); 3.34 (*q*, $J(9,10) \approx J(9,8a) \approx J(9,8b) = 4.3$, H–C(9)); 3.22 (*dd*, $J(1,3) = 2.5$, $J(1,4) = 1.0$, H–C(1)); 2.17 (2 partially superimposed *m*, $H_a$–C(8), $H_b$–C(8)); 1.70 (*dq*, $J(13,14) = 7.3$, $J(13,12) = 6.6$, 2 H–C(13)); 0.97 (*t*, $J(14,13) = 7.3$, 3 H–C(14)). MS: 230 (3, $M^+$), 215 (5, $[M - CH_3]^+$), 201 (10, $[M - C_2H_5]^+$), 187 (7), 173 (10), 165 (14), 137 (26), 129 (28), 109 (7.1), 95 (86), 91 (66), 78 (100). HR-MS: 215.1069 ($C_{14}H_{15}O_2$, calc. 215.1072).

5. *Rogiolenyne B* (= *(−)-(2*R*,*3*R*,*4*R*,*5*R*,*7*S*)*-3-(Bromomethyl)-5-chloro-7-[(*Z*)*-1-chlorohex-3-en-5-ynyl]-2-ethyloxepan-4-ol*; (−)-**4a**). Colorless oil. $[\alpha]_D = -5.0$ ($c = 0.10$, MeOH). $^1H$-NMR ($CDCl_3$): 6.13 (*dtd*, $J(4,3) = 10.8$, $J(4,5a) \approx J(4,5b) = 7.3$, $J(4,1) = 0.8$, H–C(4)); 5.60 (*ddt*, $J(3,4) = 10.8$, $J(3,1) = 2.5$, $J(3,5a) \approx J(3,5b) = 1.5$, H–C(3)); 4.57 (*dq*, $J(10,9) \approx J(10,11) = 3.9$, $J(10,8a) = 1.7$, H–C(10)); 4.37 (*ddt*, $J(9,10) = 3.9$, $J(9,8a) = 5.9$, $J(9,11) \approx J(9,8b) = 1.7$, H–C(9)); 4.29 (*dt*, $J(7,6) \approx J(7,8a) = 3.3$, $J(7,8b) = 11.5$, H–C(7)); 4.19 (*ddd*, $J(12,11) = 0.9$, $J(12,13a) = 6.4$, $J(12,13b) = 7.7$, H–C(12)); 3.90 (*ddd*, $J(6,7) = 3.4$, $J(6,5a) = 4.5$, $J(6,5b) = 9.0$, H–C(6)); 3,87, 3.68 (2 *dd*, $J(15a,11) = 10.4$, $J_{gem} = 10.7$ and $J(15b,11) = 4.4$, $J_{gem} = 10.7$, resp., 2 H–C(15)); 3.13 (*dd*, $J(1,3) = 2.5$, $J(1,4) = 0.8$, H–C(1)); 2.99 (*ddd*, $J(8b,7) = 11.5$, $J(8b,9) = 1.7$, $J_{gem} = 15.7$, $H_b$–C(8)); 2.88 (*m*, 2 H–C(5)); 2.16 (*dddd*, $J(11,10) = 3.9$, $J(11,15a) = 4.4$, $J(11,12) = 1.3$, $J(11,15b) = 10.4$, H–C(1)); 1.87 (*ddd*, $J(8a,7) = 3.1$, $J(8a,9) = 5.9$, $J_{gem} = 15.7$, $H_b$–C(8)); 1.82, 1.54 (2 *ddq*, $J(13a,12) = 7.7$, $J_{gem} = 15.6$, $J(13a,14) = 7.1$ and $J(13b,12) = 1,5$, $J_{gem} = 15.6$, $J(13b,14) = 6.4$, resp. 2 H–C(13)); 1.91 (*d*, $J(OH,10) = 4.3$, OH); 0.99 (*t*, $J = 14,13a) = J(14,13b) = 7.1$, 3 H–C(14)): MS: 348, 346 (1.5, 1, $[M - HCl]^+$); 305, 303 (3, 9, $[M - Br]^+$); 273, 271, 269 (5, 27, 20, $[M - C_6H_6Cl]^+$); 235, 233 (20, 28, [269 – HCl]$^+$); 107 (83); 91 (100).

6. *Rogiolenyne C (= (−)-(2R*,3S*,4R*,5R*,7S*)-3-(Bromomethyl)-5-chloro-7-chloro-7-[(Z)-1-chloro-hex-3-en-5-ynyl]-2-ethyloxepan-4-yl Acetate;* (−)-**4b**). Colorless oil. $[\alpha]_D = -4.0$ ($c = 0.12$, MeOH). UV (MeOH): 230 (sh, 12000), 221 (16200), 212 (sh, 12000). $^1$H-NMR ($CDCl_3$): 6.13 (*dtd*, $J(4,3) = 11.0$, $J(4,5a) \approx J(4,5b) = 7.3$, $J(4,1) = 0.9$, H–C(4)); 5.59 (*ddt*, $J(3,4) = 11.0$, $J(3,1) = 2.5$, $J(3,5a) \approx J(3,5b) = 1.4$, H–C(3)); 5.64 (*ddd*, $J(10,9) = 3.9$, $J(10,11) = 2.7$, $J(10,8a) = 1.7$, H–C(10)); 4.41 (*ddt*, $J(9,10) = 3.9$, $J(9,8a) = 5.8$, $J(9,11) \approx J(9,8b) = 1.7$, H–C(9)); 4.34 (*ddd*, $J(7,6) = 2.3$, $J(7,8a) = 3.0$, $J(7,8b) = 10.3$, H–C(7)); 4.16 (*ddd*, $J(12,11) = 0.9$, $J(12,13a) = 6.5$, $J(12,13b) = 7.5$, H–C(12)); 3.89 (*ddd*, $J(6,7) = 2.3$, $J(6,5a) = 5.6$, $J(6,5b) = 11.1$, H–C(6)); 3.86, 3.67 (2*dd*, $J(15a,11) = 10.4$, $J_{gem} = 10.6$ and $J(15b,11) = 4.1$, $J_{gem} = 10.6$, resp., 2 H–C(15)); 3.13 (*dd*, $J(1,3) = 2.5$, $J(1,4) = 0.9$, H–C(1)); 2.90 (*m*, 2 H–C(5)); 2.87 (*ddd*, $J(8b,7) = 10.3$, $J(8b,9) = 1.5$, $J_{gem} = 15.8$, $H_b$–C(8)); 2.16 (*dddd*, $J(11,10) = 2.7$, $J(11,15a) = 10.4$, $J(11,12) = 1.7$, $J(11,15b) = 4.1$, H–C(11)); 1.84 (*ddd*, $J(8a,7) = 3.0$, $J(8a,9) = 6.3$, $J_{gem} = 15.8$, 2H–C(8)); 1.81, 1.49 (2*ddq*, $J(13a,12) = 1.5$, $J_{gem} = 15.6$, $J(13a,14) = 7.5$, $J(13b,12) = 1.5$, $J_{gem} = 15.6$, $J(13b,14) = 7.5$, resp., 2 H–C(13)); 2.10 (*s*, $CH_3CO$); 0.99 (*t*, $J(14,13a) = J(14,13b) = 7.5$, 3 H–C(14)). MS: 428, 426, 424 (0.6, 1.1, 0.8, $M^+$); 392, 390, 388 (4, 17, 11, $[M - HCl]^+$); 347, 345 (13, 18, $[M - Br]^+$); 331, 329 (11, 8); 315, 313, 311 (8, 31, 27, $[M - C_6H_6Cl]^+$); 295, 293 (10, 11, $[315 - H_2O]^+$); 217, 215 (10, 11); 103 (32); 91 (36); 43 (100). HR-MS: 388.0413 ($C_{17}H_{22}BrClO_3$, calc. 388.0440).

7. *Treatment of (−)-***4b** *with Base.* A suspension of (−)-**4b** (0.003 g) in 3% $K_2CO_3$/MeOH (1 ml) was stirred at r.t. After 1 h, TLC only revealed the presence of (−)-**1**. After further stirring of this mixture for 24 h, (−)-**1** and (−)-**2** were present in a *ca.* 1:1 ratio. Workup as in *Exper. 4* led to (−)-**1** and (−)-**2**.

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