7. Coralloidolide A and Coralloidolide B, the First Cembranoids from a Mediterranean Organism, the Alcyonacean *Alcyonium coralloides*[1])

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Dedicated to the memory of Prof. *Gabriello Illuminati*

(16.X.86)

The alcyonacean *Alcyonium* (= *Parerythropodium*) *coralloides* (PALLAS, 1766) is the first Mediterranean organism shown to contain cembranoids. These are of unusual type like coralloidolide A (= (–)-(1R*,2R*,3R*,12S*,5Z,7Z,9Z)-1,2:7,10-diepoxy-12-isopropenyl-5,9-dimethylcyclotetradeca-5,7,9-triene-1,3-carbolactone; (–)-6) and coralloidolide B (= (–)-(1R*,2S*,3R*,7S*,10S*,12S*,5Z,8Z)-2,7:7,10-diepoxy-1,10-dihydroxy-12-isopropenyl-5,9-dimethylcyclotetradeca-5,8-diene-1,3-carbolactone; (–)-8). Structural assignments are mainly based on 1D- and 2D-NMR data and on chemical transformations.

1. Introduction. – A plethora of marine cembranoids, structurally similar to those isolated from both terrestrial plants and insects, *i.e.* strictly based on skeleton **1** [1a], have been isolated during the last decade from tropical Anthozoa belonging to the orders Alcyonacea and Gorgonacea. The area has been reviewed from structural and biogenetic [1] as well as synthetic points of view [2]. Such animals have also given a few unusual cembranoids, bearing furano and butenolide (or epoxylactone) moieties. This is the case of pukalide ((+)-**2**), isolated from the Hawaiian alcyonacean *Sinularia abrupta* [3a] and of 11β,12β-epoxypukalide, isolated from the western Atlantic gorgonian *Leptogorgia setacea* [3b]. The latter compound is closely related to the strongly bioactive cembranoid lophotoxin ((+)-**3**), isolated from various gorgonians of the genus *Lophogorgia* of tropical Pacific [4].
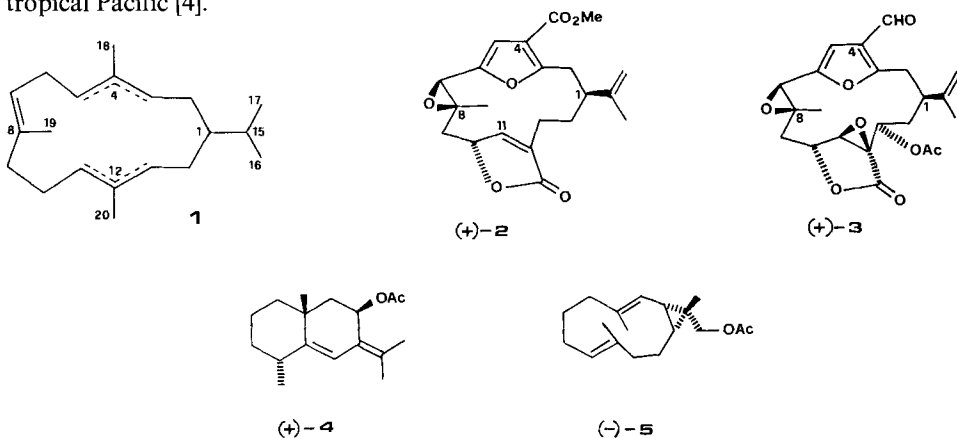
We report here on two new, unusual cembranoids isolated from Mediterranean collections of the alcyonacean *Alcyonium* (= *Parerythropodium*) *coralloides* (PALLAS, 1766). This animal has previously given two new sesquiterpenoids, the eudesmane coralloidin A ((+)-**4**) and the bicyclogermacrene coralloidin B ((−)-**5**) [5]. One of the new cembranoids bears some resemblance to 11*β*, 12*β*-epoxypukalide [3b] though having the additional feature of the rare (7*Z*)-configuration. The other new cembranoid has, in addition, peculiar O-bridges making it unique in its compound class.

2. Results and Discussion. – The first compound isolated from *A. coralloides,* coralloidolide A ((−)-**6**), has the composition $C_{20}H_{24}O_4$ (HR-MS), implying 9 unsaturations. MS-MS experiments (B/E-linked scans [6]) reveal the primary loss of 1 O-atom from the molecular ion, suggesting an epoxide group. In agreement with the MS, ^{13}C-NMR spectra *(Table 1;* multiplicities and assignment of H-bearing C-atoms from either APT [7] or HETCOR experiments [8]) show signals for 20 magnetically non-equivalent C-atoms. At low field, there is a *s* for an ester (or lactone) CO group, whilst in the olefinic region there are 1 *t*, 2 *d*, and 5 *s*. This is only compatible with a set of 1 tetrasubstituted, 2 trisubstituted, and 1 1,1-disubstituted olefinic groups owing to the absence of strong couplings between the olefinic protons *(Table 2)*. Consequently, the compound must be tetracyclic.

Two cycles must be represented by an *α,β*-epoxy-*γ*-lactone owing to both a CO IR absorption at 1785 cm^{-1} [3b] [4] [9] and ^{13}C-NMR signals *(Table 1)* typical of a

Table 1. *^{13}C-NMR Data for Coralloidolide A ((−)-6), Coralloidolide B ((−)-8), and Compound 9*[a])

C-Atom	(−)-**6**	(−)-**8**	**9**
C(1)	44.06 (*d*)	46.75 (*d*) [1.4]	46.67 (*d*)
C(2)	31.04 (*t*)	40.10 (*t*) [2.1]	40.15 (*t*)
C(3)	148.59 (*s*)[b])	113.13 (*s*) [7.8]	117.06 (*s*)
C(4)	116.95 (*s*)	143.50 (*s*) [1.4]	137.94 (*s*)
C(5)	113.44 (*d*)	126.75 (*d*) [1.8]	131.58 (*d*)
C(6)	150.11 (*s*)[b])	110.48 (*s*) [3.4]	108.73 (*s*)
C(7)	117.90 (*d*)	126.62 (*d*) [2.3]	125.49 (*d*)
C(8)	128.06 (*s*)[c])	134.75 (*s*) [1.1]	135.32 (*s*)
C(9)	36.38 (*t*)	32.41 (*t*) [1.0]	29.76 (*t*)[d])
C(10)	76.87 (*d*)	80.07 (*d*) [2.0]	90.18 (*d*)
C(11)	61.40 (*d*)	75.50 (*d*) [1.9]	77.92 (*d*)
C(12)	60.96 (*s*)	80.44 (*s*) [2.9]	84.20 (*s*)
C(13)	22.08 (*t*)	32.69 (*t*) [2.0]	35.63 (*t*)[d])
C(14)	28.21 (*t*)	26.39 (*t*) [1.1]	24.41 (*t*)
C(15)	145.02 (*s*)[a])	148.61 (*s*) [0.5]	150.15 (*s*)
C(16)	113.28 (*t*)	110.06 (*t*) [0.4]	109.05 (*t*)
C(17)	19.67 (*q*)	18.80 (*q*) [0.1]	19.34 (*q*)
C(18)	9.35 (*q*)	11.23 (*q*) [1.2]	11.32 (*q*)
C(19)	24.52 (*q*)	26.48 (*q*) [0.2]	28.08 (*q*)
C(20)	172.33 (*s*)	176.50 (*s*) [3.0]	172.95 (*s*)[e])

[a]) Solvents and concentrations as in *Table 2;* in brackets, *Δδ* values obtained on addition of an equimolar amount of Eu(fod)$_3$. The numbering of the cembrene skeleton is used, see **1**.
[b]) These resonances can be interchanged.
[c]) In (CD$_3$)$_2$CO (submerged by the solvent signals in C$_6$D$_6$).
[d]) These resonances can be interchanged.
[e]) COOMe at 57.15 (*q*); 3 MeO at 52.01 (*q*), 51.94 (*q*), and 49.39 (*q*).

Table 2. ¹H-NMR Data for Coralloidolide-A ((−)-6), Coralloidolide-B ((−)-8), and Compound 9ᵃ)

H-Atom	(−)-6ᵇ)	(−)-8ᵇ)ᵈ)	9ᵇ)ᶜ)
H−C(1)	2.58 (br. ddd, $J(1,2b) = 12.0$, $J(1,2a) = 3.5$, $J(1,14b) = 12.0$, $J(1,14a)$ and $J(1,16b)$ smallᶜ))	2.00 (br. dd, $J(1,2a) = J(1,14b) = 9.0$, $J(1,16b)$ smallᶜ)) [3.52 (br. dd)]	submerged
Hₐ−C(2)	2.39 (br. dd, $J_{gem} = 15.5$, $J(2a,1) = 3.5$, $J(2a,18) = 1.4$)	submerged [3.68 (dd, $J_{gem} = 14.0$, $J(2a,1) = 9.0$]	submerged
Hᵦ−C(2)	2.25 (dd, $J_{gem} = 15.5$, $J(2b,1) = 12.0$)	submerged [3.25 (d, $J_{gem} = 14.0$)]	submerged
H−C(5)	5.73 (br. s, $J(5,18)$ smallᶜ))	5.63 (q, $J(5,18) = 1.3$) [6.79 (br. s)]	6.02 (br. s)
H−C(7)	5.78 (br. q, $J(7,19) = 1.5$, $J(7,9b)$ smallᶜ))	5.26 (m, $J(7,19) = 1.7$, $J(7,9b) = 2.2$, $J(7,9a) = 1.0$) [6.27 (br. s)]	5.51 (br. s)
Hₐ−C(9)	2.20 (br. dd, $J_{gem} = 12.6$, $J(9a,10) = 4.5$, $J(9a,19)$ smallᶜ))	2.33 (ddd, $J_{gem} = 12.5$, $J(9a,10) = 6.0$, $J(9a,7) = 1.0$) [2.98 (br. dd)]	2.35 (br. d, $J_{gem} = 17.0$)
Hᵦ−C(9)	3.60 (br. dd, $J_{gem} = 12.6$, $J(9b,10) = 12.6$, $J(9b,7)$ smallᶜ))	2.91 (br. dd, $J_{gem} = 12.5$, $J(9b,10) = 11.2$, $J(9b,7) = 2.2$, $J(9b,19) = 0.8$) [4.01 (br. dd)]	2.65 (dd, $J_{gem} = 17.0$, $J(9b,10) = 4.5$)
H−C(10)	4.30 (dd, $J(10,9b) = 12.6$, $J(10,9a) = 4.5$)	4.86 ($dddd$, $J(10,9b) = 11.2$, $J(10,9a) = 6.0$, $J(10,11) = 4.2$) [5.79 ($dddd$)]	3.71 (br. d, $J(10,9b) = 4.5$)
H−C(11)	3.58 (s)	4.46 (d, $J(11,10) = 4.2$) [5.83 (d)]	4.43 (br. s)
Hₐ−C(13)	1.44 (ddd, $J_{gem} = 15.3$, $J(13a,14b) = 4.9$, $J(13a,14a) = 3.0$)	1.55 (ddd, $J_{gem} = 15.0$, $J(13a,14b) = J(13a,14a) = 3.5$) [3.45 (br. s, $w_{½} = 15$)]	submerged
Hᵦ−C(13)	2.76 (ddd, $J_{gem} = 15.3$, $J(13b,14a) = 13.1$, $J(13b,14b) = 2.5$)	1.93 (partially submerged) [3.45 (br. s, $w_{½} = 15$)]	submerged
Hₐ−C(14)	0.84 (br. ddd, $J_{gem} = 14.0$, $J(14a,13b) = 13.1$, $J(14a,13a) = 3.0$, $J(14a,1)$ smallᶜ))	submerged [3.05 ($dddd$, $J_{gem} = 15.0$, $J(14a,13a) = J(14a,13b) = 3.5$]	submerged
Hᵦ−C(14)	1.20 (br. ddd, $J_{gem} = 14.0$, $J(14b,1) = 12.0$, $J(14b,13b) = 2.5$, $J(14b,13a) = 4.9$)	submerged [2.20 (m)]	submerged
Hₐ−C(16)	4.96 (dq, $J_{gem} = 1.5$, $J(16a,17) = 1.5$)	4.59 (m) [4.70 (br. s)]	4.58 (br. s)
Hᵦ−C(16)	5.00 (br. dq, $J_{gem} = 1.5$, $J(16b,17) = 0.8$, $J(16b,1)$ smallᶜ))	4.66 (m) [5.06 (br. s)]	4.70 (br. s)
3 H−C(17)	1.58 (dd, $J(17,16a) = 1.5$, $J(17,16b) = 0.8$)	1.86 (dd, $J(17,16b) = 0.9$, $J(17,16a) = 1.5$) [1.98 (s)]	1.79 (br. s)
3 H−C(18)	1.66 (br. d, $J(18,2a) = 1.4$, $J(18,5)$ smallᶜ))	1.73 (d, $J(18,5) = 1.3$) [2.52 (s)]	1.69 (br. s)
3 H−C(19)	1.37 (br. d, $J(19,7) = 1.5$, $J(19,9a)$ smallᶜ))	1.66 (dd, $J(19,7) = 1.7$, $J(19,9b) = 0.8$) [1.78 (s)]	1.62 (br. s)

ᵃ) Concentrations: 0.004 g of (−)-6 in 0.5 ml of C_6D_6, 0.004 g of (−)-8 in 0.5 ml of $CDCl_3$, and 0.001 g of 9 in 0.5 ml of $CDCl_3$; in brackets, $\Delta\delta$ values obtained on addition of an equimolar amount of $Eu(fod)_3$. The numbering of the cembrene skeleton is used, see 1.

ᵇ) All couplings obtained from the monodimensional experiments were confirmed by COSY, with 0.1 sec delay before and after the second 90° pulse, in order to emphasize small couplings. The coupling patterns were derived from double irradiations.

ᶜ) The notation 'small' indicates sharpening of the signal, implying coupling constants smaller than 0.5 Hz.

ᵈ) In addition 2.73 (br. s, [10.82 (br. s)], OH−C(3)) and 2.52 (br. s, [7.91 (br. s)], OH−C(12)).

ᵉ) In C_6D_6: 4 s for MeO at 3.49, 3.33, 3.10, and 3.04.

trisubstituted epoxide (61.40 (*d*) and 60.96 (*s*) ppm) and of a γ-lactone (172.33 (*s*, *C*(=O)OC) and 76.87 (*d*, C(=O)O*C*)). This is in accordance with the ¹H-NMR spectrum *(Table 2)* which shows a *s* at 3.58 and a *dd* at 4.30 ppm for the protons at the β and γ positions, respectively, in the lactone moiety. These two protons, though being related by a 8% differential, positive NOE effect, bear no appreciable mutual coupling, thus requiring a dihedral angle of 90°. Such an angle is obtained with *Dreiding* models when the γ-substituent is *trans*-positioned to the O-atom of the epoxy moiety, as shown in fragment **A**. This interpretation is supported by the comparison with the spectral data for known α,β-epoxy-γ-lactones such as two intermediates of the synthesis of cerulenin [9], lophotoxin [4], and 11β,12β-epoxypukalide [3b].

A   **B**
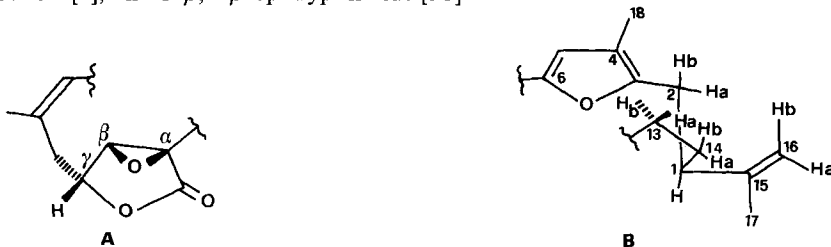
The structure of the epoxylactone can be extended at C(γ) as shown in **A** on the basis of the NMR couplings (derived from either 1D or COSY [10] experiments) of the H−C(γ) with the adjacent CH₂ group and of the CH₂ group with both the CH₃ group and the olefinic proton *(Table 2)*. The (*Z*)-configuration at the olefinic bond rests on the deshielding of the CH₃ group (24.52 ppm) [11] and on a 12% differential, positive NOE effect between the CH₃ group and the olefinic proton.

Fragment **B** (numbering of coralloidolide A ((−)-**6**)) is derived from the NMR data in *Tables 1* and *2*. The α,α-disubstituted β-methylfuran moiety, though failing to give a positive *Ehrlich* test, is revealed by the typical ¹³C-NMR (148.59, 116.95, 113.44, 150.11, and 9.35 for C(3), C(4), C(5), C(6), and C(18), resp.) and ¹H-NMR (1.66 and 5.73 for 3 H−C(18) and H−C(5)) signals [11]. This is further supported by a 15% differential, positive NOE between H−C(5) and 3 H−C(18).

The furan moiety can be extended as in fragment **B** since the groups 3 H−C(18) and Hₐ−C(2) are mutually coupled. The next group must be a CH since both protons at C(2) appear as *dd*. The other substituents at C(1) are suggested to be a CH₂CH₂ and an isopropenyl group by the data in *Table 2*²). These data also show that the isopropenyl group must be isolated from the remaining 3 olefinic groups. The latter constitute a conjugated system accounting for the strong UV absorptions in the 290-nm zone. This prompts us to join C(6) of fragment **B** with the olefinic C-atom of fragment **A** with full coplanarity of the 3 double bonds, thus obtaining a chromophore which is precedented in linear molecules [12] [13]. This is confirmed by a 2% differential, positive NOE effect between H−C(5) and the olefinic proton of fragment **A**. Moreover, though the MS fragmentation for coralloidolide A is scarcely informative, as expected for a cembranoid [1a], the ion at *m/z* 148 (C₁₀H₁₂O) may be considered to arise from bond breaking at both

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²)   This is confirmed by (*i*) double irradiation at 1.58 (*dd*, 3 H−C(17)), whereby Hₐ−C(16) and H_b−C(16) appear
     as a *d* (J_{gem} = 1.5) and a *dd* (J_{gem} = 1.5, *J*(16b,1) < 0.5), resp. (*ii*) a 6% NOE between H_b−C(16) and H−C(1),
     and (*iii*) by COSY correlation maps of H_b−C(16) with H−C(1) and of 3 H−C(17) with both protons at C(16).

the C(1)–C(2) and the C(γ)–CH$_2$ bonds. This constitutes further evidence for the furanoid portion.

According to this analysis, we are now forced to join C(13) of fragment **B** with C(α) of fragment **A** obtaining the cembranoid (−)-**6** which is drawn in the conformation best accounting for the above spectroscopic data. The C(14)–C(1)–C(2) portion is properly described by a cyclohexane-like chair arrangement with an equatorial isopropenyl substituent, in view of the large diaxial couplings of H–C(1) with both H$_b$–C(2) and H$_b$–C(14). However, the cyclohexane-structure analogy ends here as the pseudo-equatorial H$_a$–C(14) shows a large coupling constant typical for an antiperiplanar arrangement with an adjacent proton (H$_b$–C(13)) which must be positioned 'endo' with respect to the macrocycle. As regards the opposite portion of the molecule, the strong coupling between H$_b$–C(9) and H–C(10), suitable for a mutual antiperiplanar arrangement, supports conformation (−)-**6**. This compound resembles both the 11β,12β-epoxide of (+)-**2** [3b] and compound (+)-**3** [4], though it additionally bears the rare feature [14] [15] of the (7Z)-configuration.

(−) – 6   7
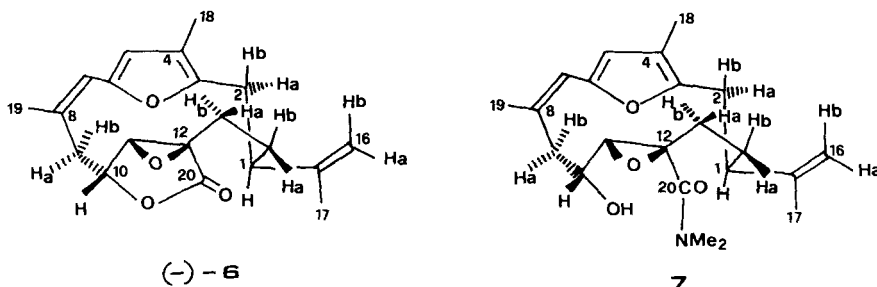
In an unsuccessful attempt to define the absolute configuration of (−)-**6** by generating a secondary-alcohol group at C(10) and then applying the *Horeau* method, (−)-**6** was reacted with Me$_2$NH in Et$_2$O. Though there is NMR evidence (see *Exper. Part*) for the formation of the expected amide **7**, somewhat surprisingly this is an ephemeral compound which loses the Me$_2$N group to give the epoxylactone (−)-**6** back. The driving force for the intramolecular replacement of the poorly nucleofugic Me$_2$N group is to be attributed to the close proximity of the nucleophile (OH) to the reaction center (C(20)) in amide **7**.

The second compound isolated from *A. coralloides,* coralloidolide B ((−)-**8**), has 20 magnetically nonequivalent C-atoms like coralloidolide A ((−)-**6**; *Table 1;* assignments of the H-bearing C-atoms based on HETCOR experiments [8]). However, HR-MS data indicate that there are 2 O- and 2 H-atoms more than in (−)-**6**, *i.e.* the composition is C$_{20}$H$_{26}$O$_6$, requiring 8 unsaturations. Moreover, the UV (λ_{max} 214 nm) and IR spectra ($\tilde{\nu}_{max}$ 3420, 3320, and 1770 cm^{-1}) show that (−)-**8** neither has the double-bond conjugation nor the oxirane ring of coralloidolide A ((−)-**6**), whilst there are OH groups which are not present in (−)-**6**.

The ^{13}C-NMR spectrum of (−)-**8** reveals a lactone CO group, 6 olefinic C-atoms (1 *t* for a terminal CH$_2$, 2 *d*, and 3 *s*), 8 non-hetero-substituted saturated C-atoms, and saturated C-atoms bearing either 1 (75.50, 80.07, and 80.44 ppm) or 2 O-atoms (110.48 and 113.13 ppm). The IR and ^{1}H-NMR spectra *(Table 2)* indicate the presence of a

(−)-8   9   C
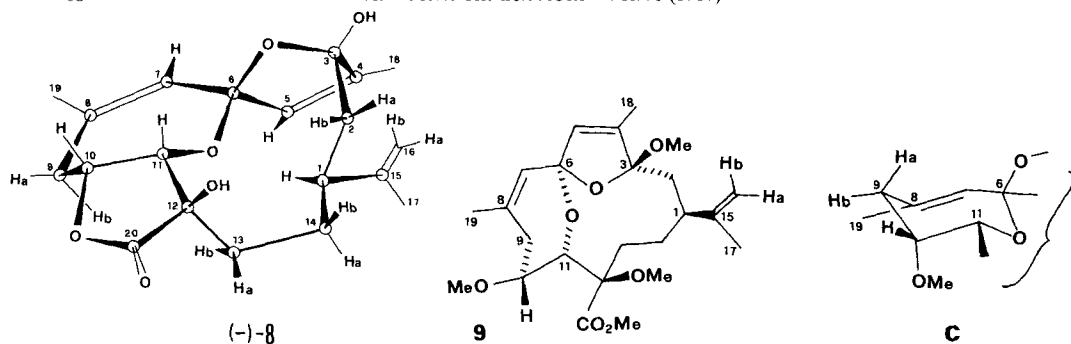
γ-lactone ring and of 2 OH functions. That these groups and the remaining 2 O-atoms are embodied in structure (−)-**8** can be deduced as follows. The terminal CH_2 group must be part of an isopropenyl group bound to C(1) as deduced from decoupling experiments *(Table 2)* and a differential, positive 9% NOE at H−C(1) on irradiation of H_b−C(16). The coupling patterns in *Table 2* support the fragments C(18)–C(4)–C(5), C(7)–(CH$_3$(19))–C(8)–C(9)–C(10)–C(11), and C(16)–C(15)–C(17), whilst the (Z)-configuration at C(7)–C(8) rests on the low-field resonance of C(19) (26.48 ppm) [11]. Moreover, the coupling patterns in *Table 2* in the presence of Eu(fod)$_3$ establish the fragment C(13)–C(14)–C(1)–C(2) whose signals without added shift reagent could not be analyzed even at high magnetic field. That C(2) is connected to C(4) *via* C(3), whilst C(11) is connected to C(13) *via* C(12), is supported by large ^{13}C-NMR Eu(fod)$_3$-induced shifts at both C(3) and C(12), which must, therefore, bear an OH group *(Table 1 and 2)*. That C(5) is connected to C(7) *via* C(6) rests on a differential, positive 6% NOE between H−C(5) and H−C(7) as well as on the simplification of the C(6) resonance on selective decoupling of either one of the protons H−C(5), H−C(7), or H−C(11). This supports also the O-bridge between C(6) and C(11), whilst the O-bridge between C(3) and C(6) rests on the low field ^{13}C-NMR signals of C(3) and C(6).

The configuration at C(3) and C(6) as shown in (−)-**8** is suggested by the above mentioned 6% NOE between H−C(5) and H−C(7). Should the configuration be inverted at both centers, with the C(5)=C(4) bond moiety taking the place of the O-bridge, a positive NOE would have been rather expected at H−C(11) and/or H−C(10) on irradiation of H−C(5), contrary to what has actually been observed. In either case, inversion at C(3) with the OH group taking the position of C(2) would be attended by too much strain.

These conclusions are reinforced by data on compound **9**, obtained by methylation of (−)-**8** with KOH/MeI [16]. Thus, ^{13}C- and ^{1}H-NMR spectra for **9** reveal the expected [17] downfield shifts for the sp^3-hybridized MeO-substituted C-atoms (C(3), C(10), and C(12)) and the expected upfield shift of H−C(10) with respect to compound (−)-**8**. It must be noted that, in contrast with coralloidolide B ((−)-**8**), there is no strong coupling between H−C(10) of **9** and either one of the protons at C(9). This suggests that compound **9** is more flexible than (−)-**8**, the seven-membered oxacycle adopting the chair-like conformation **C**, where H−C(10) forms a small dihedral angle with either proton at C(9).

A plausible biogenetic route to coralloidolide B ((−)-**8**) from coralloidolide A ((−)-**6**) is sketched in the *Scheme*. The (7Z)-configuration found for compounds (−)-**6** and (−)-**8** of *A. coralloides* is a rare feature of cembranoids, the only marine precedent of which is

(–)-**6** → [structures] → (–) - **8**
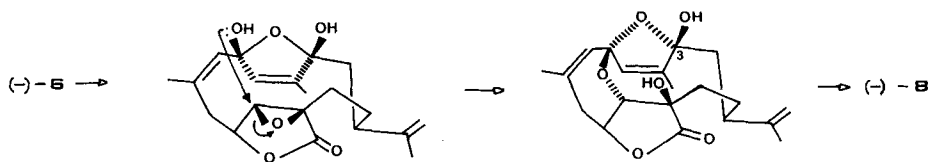
isolophodione ((–)-**10**), which was isolated from the gorgonian *Lophogorgia alba* of Pacific Mexican waters [15]. The (7*Z*)-configuration is also a rare feature of terrestrial cembranoids, a case in point being compound (–)-**11**, which was isolated from the Australian plant *Eremophila georgei* [14]. Finally, remembering that the realm of marine cembranoids are tropical waters, it is remarkable that the first cembranoids isolated from a Mediterranean organism[3]) have such peculiar structures as (–)-**6** and (–)-**8** which makes *A. coralloides* to rival with its tropical congeners in terms of biosynthetic ability.
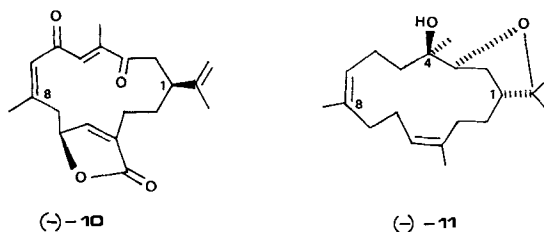
(–)-**10**   (–) -**11**

Experimental Part

1. *General.* All evaporations were carried out at reduced pressure. Column chromatography: *Merck Kieselgel 60* 63–200 µm. Flash chromatography: *Merck RP-18 LiChroprep* 40–65 µm. HPLC: *Merck-LiChrosorb Si-60* (7 µm), *Merck-LiChrosorb CN* (7 µm), or *Merck-LiChrosorb RP8* (7 µm); 25 × 1 cm columns. Polarimetric data: *JASCO-DP-181* polarimeter. UV (λ_{max} in mn, ε in $mol^{-1} l cm^{-1}$): *Beckman-DB-4*. IR ($\tilde{v}_{max}$ in cm^{-1}): *Perkin-Elmer-337*. MS (EI; *m/z* (%)): home-built spectrometer based on either a *ELFS-4-162-8-Extranuclear* quadrupole or a *VG-ZAB2F* spectrometer. NMR: *Varian-XL-300*; ^{13}C-NMR at 75.43 MHz, ^{1}H-NMR at 300 MHz; δ (ppm) relative to internal Me$_4$Si (= 0 ppm) and *J* in Hz.

2. *Isolations. A. coralloides* was collected in July-August 1985 in the French East Pyrenean Mediterranean area (Cap l'Abeille, –25, Roches de Tavac, –25, Roches de Toreilles, –36 m), immediately freed from accompanying gorgonians and immersed in 95% EtOH together with the dead gorgonian skeleton, which was cut into small pieces. A 4-l vessel of closely packed pieces was thus obtained. The solvent was decanted and the residue was twice extracted with fresh 95% EtOH. EtOH evaporation gave an aqueous residue which was extracted with petroleum ether (40–60°). The latter was evaporated to leave 4 g of a dark, oily residue which was column-chromatographed on 450 g of silica gel (gradient elution with petroleum ether/Et$_2$O/acetone. *Coralloidolide A* ((–)-**6**) and *coralloidolide B* ((–)-**8**) were eluted with petroleum ether/Et$_2$O 6:4 and Et$_2$O/acetone 1:1, resp. Compound (–)-**6** was partially purified by HPLC on *LiChrosorb Si-60* with hexane/THF 98:2 and recovered at t_R 11 min with solvent flux 7 ml/min, monitoring at 254 nm. Complete purification was then achieved by HPLC on *LiChrosorb CN* with the same solvent mixture (5 ml/min), recovering the compound (0.005 g) at t_R 18 min. Compound (–)-**8** was flash-chromatographed with MeOH/H$_2$O 8:2. The first eluate was evaporated, and the residue was subjected to reverse-phase HPLC with MeCN/H$_2$O 45:55 (5 ml/min) monitoring at 225 nm and recovering the compound (0.016 g) at t_R 7.5 min.

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[3]) *A. coralloides* only populates either the Mediterranean or the colder North-East Atlantic waters [18].

3. *Coralloidolide A* (= (−)-(1R*, 2R*, 3R*, 12S*, 5Z, 7Z, 9Z)-1,2:7,10-Diepoxy-12-isopropenyl-5,9-di-methylcyclotetradeca-5,7,9-triene-1,3-carbolactone; (−)-6). Colourless crystals, m.p. 112–113°, $[\alpha]^{20}$ (c = 0.36, EtOH): −66.1° (589), −69.9° (577), −81.4° (546), −186.9° (435), −450.0° (365). UV (EtOH): 293.5 (9700), 281.5 (12000), 272 (sh). IR (CHCl₃): 1785. MS: 328 (100, $M^{+\cdot}$), 312 (8), 283 (5), 247 (7), 201 (9), 189 (29), 177 (19), 173 (25), 161 (21), 149 (64), 148 (72), 133 (48), 105 (37), 91 (32); primary fragments from $M^{+\cdot}$ from B/E linked scans [6] were 312 (loss of O), 283 (loss of HCO₂). HR-MS: 328.1757 ± 0.01 ($C_{20}H_{24}O_4$ calc. 328.1674), 148.0791 ± 0.01 ($C_{10}H_{12}O$, calc. 148.0888).

4. *1,2:7,10-Diepoxy-3-hydroxy-12-isopropenyl-N,N,5,9-tetramethylcyclotetradeca-5,7,9-triene-1-carboxamide* (7). For 2 h, 0.5 ml of 6M Me₂NH in Et₂O containing 1.8 mg of (−)-6 was held at 0°. The mixture was evaporated and the residue subjected to reverse-phase HPLC with MeCN/H₂O 6:4 to get 7/(−)-6. After three days at −20°, the mixture proved to contain (−)-6 only. Data for 7 derived from the (−)-6/7: ¹H-NMR (CDCl₃; for numbering, see 1): 5.98 (br. s, H−C(7)); 5.92 (s, H−C(5)); 4.87, 4.83 (2 br. s, 2H−C(16)); 4.00 (br. d, J(10,9b) = 8.3, H−C(10)); 3.22 (m, H_b−C(9)); 3.12 (d, J(11,10) = 1.3, H−C(11)); 3.18, 2.93 (2 s, Me₂N); 1.98 (br. s, 3H−C(18)); 1.90 (d, J(17,16) = 1.0, 3H−C(17)); 1.72 (br. s, 3H−C(19)); the other resonances could not be assigned owing to super-impositions.

5. *Coralloidolide B* (= (−)-(1R*, 2S*, 3R*, 7S*, 10S*, 12S*, 5Z, 8Z)-2,7:7,10-Diepoxy-1,10-dihydroxy-12-isopropenyl-5,9-dimethylcyclotetradeca-5,8-diene-1,3-carbolactone; (−)-8). Crystalline colourless powder, failing to show a defined m.p. $[\alpha]^{20}$ (c = 0.78, EtOH): −85.4° (589), −89.6° (577), −102.4° (546), −190.0° (435), −336.4° (365). UV (EtOH): 214 (2300). IR (nujol): 3420s, 3320s, 1770s, 1200m, 1170m, 1080m. MS: 362 (2, $M^{+\cdot}$), 344 (4), 317 (7), 267 (3), 203 (6), 193 (15), 179 (36), 150 (29), 95 (45), 43 (100). HR-MS: 362.1630 ± 0.01 ($C_{20}H_{26}O_6$, calc. 362.1729).

6. *Methyl (1R*, 2S*, 3R*, 7S*, 10S*, 12S*, 5Z, 8Z)2,7:7,10-Diepoxy-12-isopropenyl-1,3,10-trimethoxy-5,9-dimethylcyclotetradeca-5,8-diene-1-carboxylate* (9). To a mixture of 0.5 ml of dry DMSO, 0.05 g of KOH, and 3 Å molecular sieves was added, under N₂ with stirring, (−)-8 (0.003 g), immediately followed by MeI in excess. After 30 min, the mixture was poured into H₂O, solvent extracted, and chromatographed to get 9 (28%). MS: 404 (7, $M^{+\cdot}$ −32), 309 (1), 281 (12), 266 (1), 223 (69), 187 (43), 149 (47), 109 (77), 69 (62), 57 (57), 55 (78), 43 (100).

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