176. Novel Cembranolides (Coralloidolide D and E) and a 3,7-Cyclized Cembranolide (Coralloidolide C) from the Mediterranean Coral *Alcyonium coralloides*

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The Mediterranean alcyonacean *Alcyonium* (= *Parerythropodium*) *coralloides* (PALLAS, 1766) is shown to contain three novel diterpenes which are of biogenetic significance: the 3,7-cyclized cembranoid coralloidolide C (= (+)-(6R*,7R*,8R*,11S*,12aS*,3aE)-7,8-epoxy-3,5,6,7,8,9,10,11,12,12a-decahydro-12a-hydroxy-11-isopropenyl-1,4-dimethyl-3-oxocyclopentacycloundecene-8,6-carbolactone; (−)-**3**), the O-bridged diketonic cembranolide coralloidolide D (= (+)-(1R*,2S*,3R*,5R*,12S*,8Z)-2,5-epoxy-1-hydroxy-12-isopropenyl-5,9-dimethyl-7,10-dioxocyclotetradeca-8-ene-1,3-carbolactone; (+)-**4**), and the diketonic epoxycembranolide coralloidolide E (= (+)-(1R*,2R*,3R*,12S*,5Z,8Z)-1,2-epoxy-12-isopropenyl-5,9-dimethyl-7,10-dioxocyclotetradeca-5,8-diene-1,3-carbolactone; (+)-**5**). The latter in pyridine at r.t. undergoes a double bond shift from C(4) = C(5) to C(4) = C(18) to give the isomer (−)-**7**. Structural assignments are mainly based on 1D and 2D NMR and MS spectral data. Either coralloidolide A ((−)-**1**) or the hypothetic unsaturated 1,4-diketone **9** can be envisaged as the precursors of all coralloidolides.

1. Introduction. – We have recently reported on novel cembranolides, coralloidolide A ((−)-**1**) and B ((−)-**2**), from the Mediterranean alcyonacean *Alcyonium (= Parerythropodium) coralloides* [1]. Coralloidolide A ((−)-**1**) recalls lophotoxin, an epoxycembranolide isolated from gorgonians of the genus *Lophogorgia* of tropical Pacific [2]; coralloidolide B ((−)-**2**) is a hydroxylated analogue where an OH group has brought about ring opening of the epoxide ring in (−)-**1**.

The multifarious ability of alcyonaceans in making terpenoids was thought, before our work [1], to be limited to tropical and subtropical species. This view has now to be changed, since *A. coralloides*, a species of temperate waters, contains not only cembranolide A and B [1], but also eudesmanes [3a,b] and a bicyclogermacrane [3a].

Continuing our study of *A. coralloides*, we have now isolated three other novel diterpenoids which are of biogenetic significance. They are the 3,7-cyclized cembranoid coralloidolide C ((+)-**3**), the O-bridged diketonic cembranolide coralloidolide D ((+)-**4**), and the diketonic epoxycembranolide coralloidolide E ((+)-**5**)[1]).

2. Results and Discussion. – 2.1. *Coralloidolide C* ((+)-**3**). The structure assignment of (+)-**3** is based on extensive analyses of its ^{13}C- and ^{1}H-NMR data, combined with HETCOR and INEPT experiments, and an comparison with coralloidolide A ((−)-**1**).

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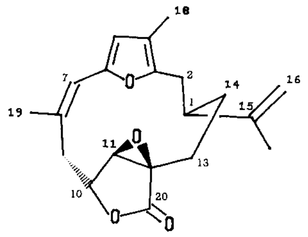
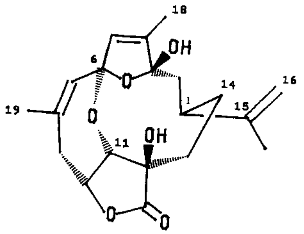
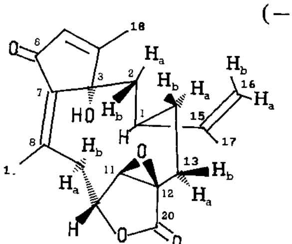
[1]) We use the cembrene numbering for the structural formulae and spectroscopic data; IUPAC nomenclature and numbering are given in the *Exper. Part*.



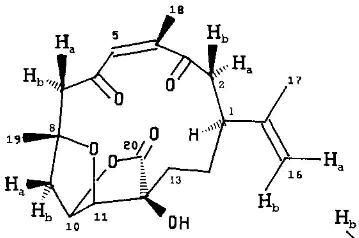
(−)-1



(−)-2



(+)-3



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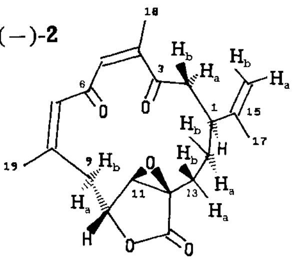

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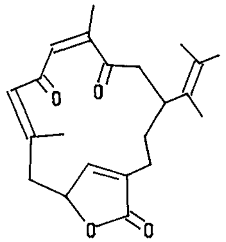

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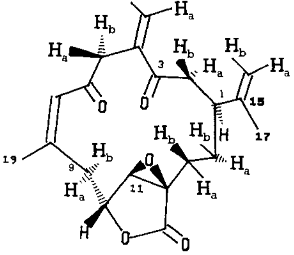


(−)-7

Table 1. *^{13}C-NMR Data for Coralloidolide C* ((+)-**3**), *Coralloidolide D* ((+)-**4**), *and Coralloidolide E* ((+)-**5**)

	(+)-**3**[a])	(+)-**4**[a])	(+)-**5**[b])
C(1)	41.39 (*d*)	45.99 (*d*)	37.61 (*d*)
C(2)	39.73 (*t*)	39.75 (*t*)	41.67 (*t*)
C(3)	81.03 (*s*)	203.47 (*s*)	205.37 (*s*)
C(4)	172.22 (*s*)	143.41 (*s*)	161.10 (*s*)
C(5)	133.67 (*d*)	136.22 (*d*)	126.13 (*d*)
C(6)	193.76 (*s*)	201.82 (*s*)	188.60 (*s*)
C(7)	138.96 (*s*)	45.03 (*t*)	126.91 (*d*)
C(8)	140.79 (*s*)	83.61 (*s*)	156.78 (*s*)
C(9)	34.96 (*t*)	56.65 (*t*)	37.45 (*t*)
C(10)	79.18 (*d*)	85.52 (*d*)	76.58 (*d*)
C(11)	60.34 (*d*)	82.51 (*d*)	64.71 (*d*)
C(12)	62.20 (*s*)	73.48 (*s*)	60.83 (*s*)
C(13)	22.85 (*t*)	33.49 (*t*)	21.11 (*t*)[c])
C(14)	35.20 (*t*)	27.32 (*t*)	22.65 (*t*)[c])
C(15)	146.21 (*s*)	150.48 (*s*)[b])	147.82 (*s*)
C(16)	113.52 (*t*)	109.66 (*t*)	110.60 (*t*)
C(17)	17.32 (*q*)	21.30 (*q*)	22.60 (*q*)
C(18)	12.65 (*q*)	12.80 (*q*)	20.91 (*q*)
C(19)	24.53 (*q*)	25.67 (*q*)	26.32 (*q*)
C(20)	172.92 (*s*)	178.29 (*s*)	172.20 (*s*)

[a]) In (D$_5$)pyridine.

[b]) In (CD$_3$)$_2$CO.

[c]) These resonances can be interchanged.

Preliminary indications as to the diterpenoidic nature of (+)-**3** come from the ^{13}C-NMR spectrum which shows twenty C-atoms. This spectrum *(Table 1)* reveals analogies with (–)-**1** [1], showing resonances for both a 2,3-epoxybutanolide system and an isopropenyl group. There are also differences, however; of special relevance is that there is only 1 sp^2 d for (+)-**3** instead of the 2 *d*'s for (–)-**1** [1]. Moreover, with (+)-**3**, there is a *s* at low field (81.03 ppm) which fits for an O-substituted tertiary C-atom and a *s* at 193.76 ppm for a C=O. No such features are present with (–)-**1** [1].

Comparing the ^{1}H-NMR spectra, (+)-**3** resembles (–)-**1** insofar as the CH$_2$(9)–CH(10)CH(11) and the isopropenyl group are concerned. Thus, the epoxybutanolide portion of (+)-**3** finds further support in a *s* at 4.61 ppm *(Table 2)*, characteristic of an epoxidic proton which is, like H–C(11), in a 90° dihedral arrangement with respect to, and thus showing no coupling with, the vicinal proton, H–C(10). The ^{1}H-NMR data *(Table 2)* support the fragment C(2)–C(1)(C(CH$_3$)=CH$_2$)–C(14)–C(13) which can be further extended to include C(12)–C(11)–C(10)–C(9)–C(8)–C(19) on the basis of observed long-range coupling of H–C(10) with H$_a$–C(13).

Long-range HETCOR experiments [4] with (+)-**3** *(Exper. Part)* serve to correlate C(20) with both protons at C(13), which further extends the structural analogy with (–)-**1**. HR-MS data reveal the molecular composition C$_{20}$H$_{24}$O$_5$ for (+)-**3** and thus 9 unsaturations. This demands one more carbocycle more than with coralloidolide A ((–)-**1**)

Table 2. *^{1}H-NMR Data for Coralloidolide C ((+)-**3**) and Coralloidolide D ((+)-**4**) in (D$_5$)Pyridine*

	(+)-**3**	(+)-**4**
H–C(1)	1.80 (br. *ddd*, J(1, 14a) = 11.0, J(1, 2a) = 4.0, J(1, 2b) = 3.5, J(1, 16b) small)	2.43 (br. *dd*, J(1, 2b) = 8.0, J(1, 2a) = 2.8, J(1, 16b) = 1.0)
H$_a$–C(2)	2.32 (*dd*, J_{gem} = 14.5, J(2a, 1) = 4.0)	2.90 (*dd*, J_{gem} = 13.0, J(2a, 1) = 2.8)
H$_b$–C(2)	2.18 (*dd*, J_{gem} = 14.5, J(2b, 1) = 3.5)	3.00 (*dd*, J_{gem} = 13.0, J(2b, 1) = 8.0)
H–C(5)	6.20 (*q*, J(5, 18) = 1.6)	7.49 (*q*, J(5, 18) = 1.0)
H$_a$–C(7)	–	2.75 (*AB*, J(*A*,*B*) = 12.5, J(7b, 19) small)
H$_b$–C(7)	–	2.95 (*AB*, J(*A*,*B*) = 12.5)
H$_a$–C(9)	2.11 (*dd*, J_{gem} = 14.0, J(9a, 10) = 4.2)	2.28 (br. *dd*, J_{gem} = 14.5, J(9a, 10) = 6.9)
H$_b$–C(9)	5.12 (*dd*, J_{gem} = 14.0, J(9b, 10) = 2.8)	2.14 (*dd*, J_{gem} = 14.5, J(9b, 10) = 2.2, J(9b, 19) small)
H–C(10)	4.98 (*ddd*, J(10, 9a) = 4.2, J(10, 9b) = 2.8, J(10, 13a) = 0.6)	5.40 (*ddd*, J(10, 9a) = 6.9, J(10, 11) = 4.6, J(10, 9b) = 2.2)
H–C(11)	4.61 (*s*)	4.85 (*d*, J(11, 10) = 4.6)
H$_a$–C(13)	2.54 (br. *dd*, J_{gem} = 14.5, J(13a, 14b) = 13.0, J(13a, 14a) = 2.0 J(13a, 10) = 0.6)	superimposed
H$_b$–C(13)	1.40 (*ddd*, J_{gem} = 14.5, J(13b, 14a) = 5.5, J(13b, 14b) = 2.0)	superimposed
H$_a$–C(14)	1.92 (*dddd*, J_{gem} = 14.0, J(14a, 1) = 11.0, J(14a, 13b) = 5.5, J(14a, 13a) = 2.0)	superimposed
H$_b$–C(14)	1.43 (*ddd*, J_{gem} = 14.0, J(14b, 13a) = 13.0, J(14b, 13b) = 2.0	superimposed
H$_a$–C(16)	4.78 (*dq*, J_{gem} = 2.6, J(16a,17) = 1.4)	4.74 (*dq*, J_{gem} = 1.7, J(16a, 17) = 1.5)
H$_b$–C(16)	5.08 (br. *dq*, J_{gem} = 2.6, J(16b, 17) = 0.6, J(16b, 1) small)	4.72 (*ddq*, J_{gem} = 1.7, J(16b, 1) = 1.0, J(16b, 17) = 0.8)
3 H–C(17)	1.65 (*dd*, J(17, 16a) = 1.4, J(17, 16b) = 0.6)	1.72 (*dd*, J(17, 16a) = 1.5, J(17, 16b) = 0.8)
3 H–C(18)	1.96 (*d*, J(18, 5) = 1.6)	2.16 (*d*, J(18, 5) = 1.0)
3 H–C(19)	2.50 (*s*)	1.21 (br. *s*, J(19, 7b) and J(19, 9b) small)

and B ((–)-**2**). The location of the additional carbocycle is revealed by long-range HETCOR experiments [4] showing the correlations C(6)/*H*–C(5), C(7)/3*H*–C(19), C(7)/H_a–C(9), C(8)/H_b–C(9), and C(8)/3*H*–C(19) (which establish the C(7)=C(8) (CH_3(19))–CH_2(9) fragment). Such experiments reveal also that C(3) is correlated with both 3 H–C(18) and H_b–C(2), which indirectly supports the CH_3(18)–C(3)(OH)–CH_2(2) fragment. All these observations can be rationalized if C(7) is connected to C(3), which finds evidence in the results of selective INEPT experiments [5]. Thus, selective irradiation at H_a–C(2) reveals that this proton is correlated with C(15), C(3), and C(7), in full support of the position of the cyclopentenone moiety in (+)-**3**.

Relative configurations of (+)-**3** rest on the following NMR evidence. The fact that H_b–C(9) resonates at particularly low field (5.12 ppm) suggests that this proton is spatially close to the OH group, thus establishing the (*E*) configuration at the C(7)=C(8) bond. Should the configuration at C(7)=C(8) be (*Z*), the 3 H–C(19) group would be deshielded by the OH group, contrary to what is observed. The configuration at C(3) is firmly based on the proximity of H–C(11) to 3 H–C(19), as revealed by a +11% NOE between 3 H–C(19) and H–C(11). The spatial position of the isopropenyl group as in (+)-**3** rests on the lack of coupling between H–C(1) and H_b–C(14) (*Table 2*), which implies a dihedral angle of 90° for H–C(1)–C(14)–H_b.

The C-skeleton of coralloidolide C ((+)-**3**) has been rarely encountered; to the best of our knowledge, only two compounds with the C-connectivity of (+)-**3** have been reported. They have been isolated from another alcyonacean: *Cespitularia* sp. of the Great Barrier [6].

2.2. *Coralloidolide D* ((+)-**4**). The structure of (+)-**4** is assigned mainly by means of its ^{13}C- and ^{1}H-NMR data and INEPT, NOE, and NOESY experiments.

The ^{13}C-NMR spectrum (*Table 1*) reveals an isopropenyl group and a lactone ring in a coralloidolide-type structure, besides 2 C=O and a trisubstituted olefinic group, whereas there is no evidence for an oxirane ring. The HR-MS indicates the composition $C_{20}H_{26}O_6$ which, in view of the above NMR observations, demands three cycles. The ^{13}C-NMR spectrum reveals also 2 *s* at 83.61 and 73.48 ppm and 2 *d* at 85.52 and 82.51 ppm for C-atoms bearing a singly bound O-atom.

The ^{1}H-NMR spectrum (*Table 2*) supports the fragments C(2)–C(1)(C(CH_3)=CH_2)–C(14)–C(13) and C(4)(CH_3)=C(5). The 3 H–C(19) protons are W coupled with both H_b–C(7) and H_b–C(9). While H_b–C(7) is part of a magnetically isolated CH_2 group, H_b–C(9) is part of a *ABX* system where the *X* part has a chemical shift of 5.40 ppm compatible with a proton of type H–C(10). The latter is further coupled with a deshielded proton which can be assigned to H–C(11). Selective INEPT experiments [5] (*Exper. Part*) show coupling of 3*H*–C(19) with deshielded C(8) (83.61 ppm) and of *H*–C(11) with both C(20) and deshielded C(11) (82.51 ppm). Deshielding of the coupled C-atoms can be rationalized with a C(8)–O–C(11) bridge.

Differential NOE's (*Exper. Part*) give further structural evidence. Irradiation at 3 H–C(19) shows enhancements of 8% on H–C(11), 6% on H_a–C(9), and 4% on H_a–C(7), thus confirming the C(8)–O–C(11) bridge. Irradiation at H_b–C(7) shows enhancements of 10% on H–C(5), which fits for the C(7)–C(6)–C(5) portion. Moreover, irradiation at 3 H–C(18) shows enhancement of 5% on H–C(5), thus establishing the (*Z*) configuration at the olefinic bond. Finally, correlation maps in NOESY experiments between H–C(10) and H–C(11) establish the *cis* fusion at C(10)–C(11).

2.3. *Coralloidolide E* ((+)-**5**). ^{13}C- and ^{1}H-NMR spectra, INEPT and NOE experiments, and comparison with coralloidolide A ((–)-**1**) and lophodione (**6**) establish structure (+)-**5** for coralloidolide E. Moreover, though stable in acetone solution, (+)-**5** undergoes chemical changes when dissolved in pyridine, partly being transformed into its double-bond isomer (–)-**7**.

As with coralloidolide C ((+)-**3**) and A ((–)-**1**), the ^{13}C-NMR spectrum (*Table 1*) of (+)-**5** reveals signals for an epoxybutanolide system. However, 2C=O signals replace those for the α-furanic C(3) and C(6) atoms of (+)-**1**. HR-MS experiments indicating the composition $C_{20}H_{24}O_5$ suggest that we are dealing with another cembranolide. Under this presumption, the 2C=O signals recall the structure of lophodione (**6**) [7] with, additionally, a 11,12-epoxy group; the latter is indicated in the ^{1}H-NMR spectrum by the typical [1] chemical shift of H–C(11).

^{1}H-NMR spectra (*Exper. Part*) support the portions from C(10) to C(7) and C(2)–C(1) (C(CH_3)=CH_2)–C(14)–C(13). Though no coupling constant values can be extracted from the ^{1}H-NMR spectrum for the C(14)–C(13) section, irradiation at H_a–C(13) reveals a small coupling with H–C(10); this serves to assign 2H–C(13).

The C(6)–C(3) portion is elucidated by means of INEPT experiments *(Exper. Part)*. Thus, irradiations at H–C(5) or H–C(7) reveal correlation of both protons with C(6)=O. Moreover, irradiation at H_a–C(2), which unavoidably leads also to irradiation at H_b–C(13), reveals correlation of H_a–C(2) with C(4), C(3), and C(15) and of H_b–C(13) with C(12).

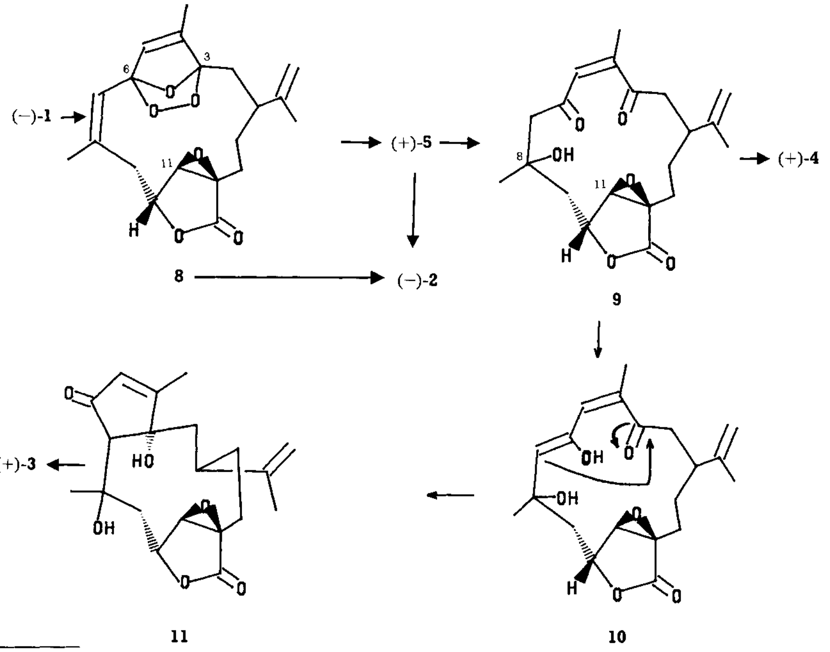
That the configuration is (*Z*) at both double bonds of the cycle rests on NOE experiments *(Exper. Part)*: 12% enhancement at H–C(5) on irradiation at 3 H–C(18) and 7% enhancement at H–C(7) on irradiation at 3 H–C(19). This further differentiates (+)-**5** from lophodione (**6**) where the C(7)=C(8) bond has (*E*) configuration. Finally, a +15% NOE between H–C(5) and H–C(7) further defines the molecular geometry of the upper portion of (+)-**5**.

The structure of the double-bond isomer (–)-**7** is immediately clear from the examination of NMR data. Thus, in the ^{13}C-NMR spectra, the *d* at 126.91 (H–C(5)) and *q* at 22.60 ppm (3 H–C(18)) of (+)-**5** change into 2 *t* at 46.92 (2 H–C(5)) and 128.45 ppm (2 H–C(18)) of (–)-**7** *(Exper. Part)*. In the ^{1}H-NMR spectra, the *q* at 6.38 and *d* at 2.02 ppm for H–C(5) and 3 H–C(18), respectively, of (+)-**5** change into 2 br. *d* at 3.72 and 3.28 ppm for 2 H–C(5) and a br. *dd* at 6.04 and a br. *d* at 6.30 ppm for 2 H–C(18) of (–)-**7** *(Exper. Part)*.

2.4. *Biogenesis.* It is known that 2,3,5-trialkylfurans can be oxidized to 2-en-1,4-diones with a variety of chemical reagents [8] or *via* photosensitized oxygenation [9] or electrolysis [10]. In turn, 2-ene-1,4-diones can be reconverted to furans on addition of $PCl_3/POCl_3$ [11]. On the basis of such chemical precedents, it is appealing to try to interrelate biogenetically the furans and unsaturated diketones isolated from *A. coralloides*.

The possibility that unsaturated diketones descend from furans is illustrated in the *Scheme*, where coralloidolide A ((–)-**1**) is imagined as the precursor of all coralloidolides by first forming, on oxygenation, the hypothetical peroxide **8** which may give both coralloidolide B ((–)-**2**) and coralloidolide E ((+)-**5**)[2]. Route (–)-**1**→**8**→(–)-**2** has al-

Scheme. *Hypothetical Biogenetic Scheme for the Coralloidolides of* A. coralloides



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[2] The endoperoxide is not mandatory to conceive oxygenation at C(3) and C(6).

ready been suggested in our previous work [1]. Present findings further suggest that (–)-**2** can also be formed directly from (+)-**5** *via* sequential OH^- attack at C(3) of (+)-**5** followed by C(3)–O^- attack at C(6) with ring closure and C(6)–O^- attack at C(11) with oxirane-ring opening. On hydration of (+)-**5**, the hypothetical intermediate **9** can be formed from which both coralloidolide D ((+)-**4**) and coralloidolide C ((+)-**3**) may arise. Process **9**→(+)-**4** involves epoxide-ring opening by C(8)–OH attack at C(11). Process **9**→(+)-**3** is conceived *via* two hypothetical intermediates: enol **10** and cyclopentenone **11**, the latter giving (+)-**3** on dehydration.

In the hypothesis that furans descent from 2-ene-1,4-diones, the hypothetical diketone **9** can be considered as the precursor of all other diterpenes of *A. coralloides.*

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Experimental Part

1. *General.* All evaporations were carried out at reduced pressure. HPLC: *Merck LiChrosorb Si–60* (7 µm) or *Merck LiChrosorb CN* (7 µm); reverse-phase HPLC, *Merck LiChrosorb RP18* (7 µm); all columns were 25 × 1 cm. Polarimetric data: *JASCO-DP-181* polarimeter. UV (λ_{max} in nm, ε in mol^{-1} l cm^{-1}): *Perkin-Elmer Lambda 3* spectrophotometer. IR ($\tilde{\nu}_{max}$ in cm^{-1}): *Pye-Unicam SP3-200S* spectrometer. NMR: *Varian-XL-300*; ^{13}C-NMR at 75.43 MHz, ^1H-NMR at 300 MHz; δ (ppm) relative to internal Me_4Si (= 0 ppm) and *J* in Hz ('small' indicates $J < 0.5$). Differential NOE: irradiated proton→% NOE on the observed proton(s). Selective INEPT: irradiated proton→observed C-atom(s). Long-range HETCOR: C-atom→proton(s). MS (EI; *m/z* (%)): *VG 70–70* spectrometer.

2. *Isolations. A. coralloides* was collected in summer 1987 in the same area, and was extracted with EtOH, as before [1]. However, this time the aq. residue from evaporation of excess EtOH was extracted first with petroleum ether and then with AcOEt. The residue from the AcOEt extract (0.4 g) was subjected to reverse-phase HPLC with $MeOH/H_2O$ 55:45 collecting three fractions at t_R 6.5, 8.2, and 10.8 min, corresponding to *coralloidolide D* ((+)-**4**; 3.0 mg), *coralloidolide C* ((+)-**3**; 4.9 mg), and *coralloidolide E* ((+)-**5**; 11.8 mg.), resp.

3. *Coralloidolide C* (= *(+)-(6*R**,7*R**,8*R**,11*S**,12a*S**,3a*E*)-7,8-Epoxy-3,5,6,7,8,9,10,11,12,12a-decahydro-12a-hydroxy-11-isopropenyl-1,4-dimethyl-3-oxocyclopentacycloundecene-8,6-carbolactone;* (+)-**3**). Colourless needles. M.p. 266° (dec.; MeOH). $[\alpha]_D^{20} = +3.1$ ($c = 0.065$, EtOH). UV (EtOH): 255 (7500), 215 (10000). IR (nujol): 3350*s*, 1770*s*, 1740v*s*. Differential NOE (C_5D_5N): H_b–C(13)→8% on H–C(11); 3 H–C(17)→6% on H_a–C(16); 3 H–C(18)→10% on H–C(5); 3 H–C(19)→11% on H–C(11). Selective INEPT (C_5D_5N): H_a–C(2)→C(15), C(7), C(3); H–C(5)→C(6), C(7); H–C(11)→C(20); 3 H–C(19)→C(7). Long-range HETCOR: C(3)→H_b–C(2), 3 H–C(18); C(4)→3 H–C(18); C(5)→3 H–C(18); C(6)→H–C(5); C(7)→3 H–C(19), H_a–C(9); C(8)→3 H–C(19), H_b–C(9); C(9)→3 H–C(19); C(10)→H_b–C(9), H–C(11); C(11)→H_b–C(9); C(15)→3 H–C(17); C(16)→3 H–C(17); C(20)→H_a–C(13), H_b–C(13). MS: 344 (21, $M^{+\cdot}$), 329 (4), 299 (6), 229 (7), 188 (26), 163 (51), 147 (33). HR-MS: 344.16252±0.004 ($C_{20}H_{24}O_5$, calc. 344.16237).

4. *Coralloidolide D* (= *(+)-(1*R**,2*S**,3*R**,5*R**,12*S**,8*Z*)-2,5-Epoxy-1-hydroxy-12-isopropenyl-5,9-dimethyl-7,10-dioxocyclotetradeca-8-ene-1,3-carbolactone;* (+)-**4**). Needles. M.p. 209–211° (EtOH). $[\alpha]_D^{20} = +41.0$ ($c = 0.105$, EtOH). UV (EtOH): 244 (5000). IR (nujol): 3350*s*, 1770*s*, 1730*s*, 1680v*s*. Differential NOE (C_5D_5N): H_a–C(2)→3% on H–C(1); H_b–C(7)→10% on H–C(5); 3 H–C(17)→2% on H_a–C(16); 3 H–C(18)→5% on H–C(5); 3 H–C(19)→8% on H–C(11), 4% on H_a–C(7), and 6% on H_a–C(9). Selective INEPT (C_5D_5N): H–C(11)→C(20) and C(11); 3 H–C(19)→C(8). MS: 362 (49, $M^{+\cdot}$), 344 (30), 334 (19), 319 (15), 253 (5), 237 (7), 209 (8), 195 (38), 163 (89), 135 (32), 123 (47), 111 (100), 95 (64); B/E on $M^{+\cdot}$ gave 344 and 334. HR-MS: 362.17325±0.004 ($C_{20}H_{26}O_6$, calc. 362.17294).

5. *Coralloidolide E* (= *(+)-(1*R**,2*R**,3*R**,12*S**,5*Z*,8*Z*)-1,2-Epoxy-12-isopropenyl-5,9-dimethyl-7,10-dioxocyclotetradeca-5,8-diene-1,3-carbolactone*; (+)-**5**). Needles. M.p. 190–192° (acetone). $[\alpha]_D^{20} = +12.8$ ($c = 0.21$, acetone). UV (EtOH): 268 (4000). IR (nujol): 1770v*s*, 1700*s*, 1620*s*. ^1H-NMR ($(CD_3)_2CO$): 3.10 (br. *d*, $J(1,2b) = 10.2$, $J(1,2a) = 2.2$, $J(1,14a) = 3.5$, $J(1,16a) = 0.6$, $J(1,17) = 0.5$, $J(1,16b)$ small, H–C(1)); 2.38 (*ddd*, $J_{gem} = 18.0$, $J(2a,1) = 2.2$, $J(2a,14a) = 1.5$, H_a–C(2)); 2.72 (*dd*, $J_{gem} = 18.0$, $J(2b,1) = 10.2$, H_b–C(2)); 6.38 (*q*, $J(5,18) = 1.5$, H–C(5)); 6.60 (*dq*, $J(7,19) = 1.5$, $J(7,9b) = 0.6$, H–C(7)); 2.65 (br. *dd*, $J_{gem} = 11.1$, $J(9a,10) = 6.2$, $J(9a,19)$ small,

H_a–C(9)); 3.77 (br. *dd*, J_{gem} = 11.1, *J*(9b,10)=11.1, *J*(9b,7)=0.6, H_b–C(9)); 4.72 (br. *dd*, *J*(10,9b) = 11.1, *J*(10,9a) = 6.2, *J*(10,13a) small, H–C(10)); 3.87 (*s*, H–C(11)); 1.90 (submerged, H_a–C(13)); 2.36 (submerged, H_b–C(13)); 1.98 (submerged, H_a–C(14)); 1.07 (*ddd*, J_{gem} = 13.8, *J*(14b,13a) = 8.7, *J*(14b,13b) = 1.2, H_b–C(14)); 4.80 (br. *dq*, J_{gem} = 1.5, *J*(16a,17) = 1.5, *J*(16a,1) = 0.6, H_a–C(16)); 4.58 (br. *dq*, J_{gem} = 1.5, *J*(16b, 17) = 0.6, *J*(16b,1) small, H_b–C(16)); 1.82 (br. *dd*, *J*(17,16a) = 1.5, *J*(17,16b) = 0.6, *J*(17,1) = 0.5, 3 H–C(17)); 2.02 (*d*, *J*(18,5) = 1.5, 3 H–C(18)); 2.12 (br. *d*, *J*(19,7) = 1.5, *J*(19,9a) small, 3 H–C(19)). Differential NOE ($(CD_3)_2CO$): H–C(5)→5% on H–C(7); H–C(7)→8% on H–C(5); 3 H–C(17)→3% on H_a–C(16); 3 H–C(18)→12% on H–C(5); 3 H–C(19)→7% on H–C(7). Selective INEPT (acetone): H–C(5)→C(6); H–C(7)→C(6); H_b–C(13) and H_a–C(2)→C(3), C(4), C(12), C(15). MS: 344 (17, $M^{+\cdot}$), 326 (7), 316 (10), 203 (15), 189 (19), 175 (33), 150 (79), 135 (54), 122 (97), 107 (83), 91 (95), 43 (100). HR-MS: 344.1655±0.004 ($C_{20}H_{24}O_5$, calc. 344.1624). B/E on $M^{+\cdot}$ gave 329, 326, and 316; B/E on *m/z* 316 gave 298 and 273.

6. *(–)-(1*R**,2*R**,3*R**,12*S**,5*Z*)-1,2-Epoxy-12-isopropenyl-5-methyl-9-methylidene-7,10-dioxocyclotetradec-5-ene-1,3-carbolactone* ((–)-**7**). The residue from evaporation of the solvent from degraded solns. of (+)-**5** in (D_5)pyridine was subjected to HPLC on a *CN* column with hexane/EtOH 84:16 (1 ml/min) to give (–)-**7** at t_R 7.9 min (t_R 12.8 for (+)-**5**). $[\alpha]_D^{20}$ = –48.9 (*c* = 0.045, EtOH). UV (EtOH): 243 (9300), 215 (7900). IR (nujol): 1785v*s*, 1740*m*, 1670*s*, 1620*s*. ^{1}H-NMR ($(CD_3)_2CO$): 2.66 (*m*, *J*(1,2b) = 11.5, *J*(1,2a) = 3.8, *J*(1,16b) = 0.9, H–C(1)); 3.12 (*dd*, J_{gem} = 12.0, *J*(2a,1) = 3.8, H_a–C(2)); 2.36 (*dd*, J_{gem} = 12.0, *J*(2b,1) = 11.5, H_b–C(2)); 3.72 (br. *d*, J_{gem} = 15.0, *J*(5a,18b) = 1.5, *J*(5a,18a) = 0.9, H_a–C(5)); 3.28 (br. *d*, J_{gem} = 15.0, *J*(5b, 18b) = 0.6, H_b–C(5)); 6.54 (br. *q*, *J* = (7,19) = 1.3, *J*(7,9a) small, H–C(7)); 2.93 (br. *dd*, J_{gem} = 12.0, *J*(9a,10) = 5.0, *J*(9a,7) small, H_a–C(9)); 3.55 (*dd*, J_{gem} = 12.0, *J*(9b,10) = 10.0, H_b–C(9)); 4.73 (*dd*, *J*(10,9b) = 10.0, *J*(10,9a) = 5.0, H–C(10)); 3.79 (*s*, H–C(11)); *ca.* 1.8 (superimposed, 2 H–C(13)); *ca.* 1.98 (superimposed, 2 H–C(14)); 4.86 (*dq*, J_{gem} = 1.8, *J*(16a,17) = 1.5, *H_a*–C(16)); 4.84 (*ddq*, J_{gem} = 1.8, *J*(16b,17) = 0.9, *J*(16b,1) = 0.9, H_b–C(16)); 1.77 (*dd*, *J*(17,16a) = 1.5, *J*(17,16b) = 0.9, 3 H–C(17)); 6.30 (br. *d*, *J*(18a,5a) = 0.9, J_{gem} small, H_a–C(18)); 6.04 (br. *dd*, *J*(18b,5a) = 1.5, *J*(18b,5b) = 0.6, J_{gem} small, H_b–C(18)); 2.05 (submerged, 3 H–C(19)). ^{1}H-NMR (C_5D_5N): 2.75 (*dddd*, *J*(1,2b) = 12.0, *J*(1,2a) = 3.5, *J*(1,14a) = 7.0, *J*(1,14b) = 3.0, H–C(1)); 3.04 (*dd*, J_{gem} = 12.0, *J*(2a,1) = 3.5, H_a–C(2)); 2.41 (*dd*, J_{gem} = 12.0, *J*(2b,1) = 12.0, H_b–C(2)); 3.78 (*dd*, J_{gem} = 15.0, *J*(5a,18b) = 1.2, H_a–C(5)); 3.24 (*d*, J_{gem} = 15.0, H_b–C(5)); 6.37 (*q*, *J*(7,19) = 1.5, H–C(7)); 2.95 (br. *dd*, J_{gem} = 12.0, *J*(9a,10) = 4.5, H_a–C(9)); 3.65 (*dd*, J_{gem} = 12.0, *J*(9b,10) = 10.0, H_b–C(9)); 4.83 (*dd*, *J*(10,9b) = 10.0, *J*(10,9a) = 4.5, H–C(10)); 4.07 (*s*, H–C(11)); 2.13 (*ddd*, J_{gem} = 15.0, *J*(13b,14b) = 8.0, *J*(13b,14a) = 6.5, H_b–C(13)); 1.98 (*ddd*, J_{gem} = 15.0, *J*(13a,14b) = 6.0, *J*(13a,14a) = 8.5, H_a–C(13)); 1.41 (*dddd*, J_{gem} = 14.0, *J*(14a,13a) = 8.5, *J*(14a,1) = 7.0, *J*(14a,13b) = 6.5, H_a–C(14)); 1.55 (*dddd*, J_{gem} = 14.0, *J*(14b,13b) = 8.0, *J*(14b,13a) = 6.0, *J*(14b,1) = 3.0, H_b–C(14)); 4.79 (br. *s*, 2 H–C(16)); 1.60 (br. *s*, 3 H–C(17)); 6.15 (br. *s*, J_{gem} small, H_a–C(18)); 5.90 (br. *d*, *J*(18b,5a) = 1.2, J_{gem} small, H_b–C(18)); 1.80 (*d*, *J*(19,7) = 1.5, 3 H–C(19)). Differential NOE ($(CD_3)_2CO$): H_a–C(2)→3% on H_a–C(18); H_b–C(2)→1% on H_b–C(16); H_a–C(5)→7% on H–C(7); H_b–C(5)→3% on H_b–C(18). ^{13}C-NMR ($(CD_3)_2CO$): 43.32 (*d*, C(1)); 40.67 (*t*, C(2)); 144.27 (*s*, C(4)); 46.92 (*t*, C(5)); 127.65 (*d*, C(7)); 151.92 (*s*, C(8)); 34.93 (*t*, C(9)); 76.27 (*d*, C(10)); 61.29 (*δ*, C(11)); 60.25 (*s*, C(12)); 20.31 (*t*, C(13)); 23.87 (*t*, C(14)); 146.59 (*s*, C(15)); 111.03 (*t*, C(16)); 19.85 (*q*, C(17)); 128.42 (*t*, C(18)); 25.19 (*q*, C(19)); signals for C(3), C(6), and C(20) not detected.

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