70. Coralloidin C, D, and E: Novel Eudesmane Sesquiterpenoids from the Mediterranean Alcyonacean *Alcyonium coralloides*

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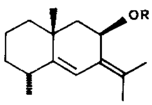
The Mediterranean alcyonacean *Alcyonium* (=*Parerythropodium*) *coralloides* (Pallas, 1766) is shown to contain the novel eudesmane sesquiterpenoids coralloidin C (=(–)-(4*R*,10*S*)-eudesma-5,7(11)-dien-15-yl acetate; (–)-**4**), coralloidin D (=(–)-(10*R**)-eudesma-4,7(11)-diene-12,13-diyl diacetate; (–)-**7**), and coralloidin E (=(+)-(4*R**,10*R**)-eudesma-5,7-dien-11-ol; (+)-**8**). The absolute configuration of (–)-**4** is derived by the exciton-coupling method, applied to deacetylcoralloidin C *p*-anisate ((–)-**6**). Coralloidin E ((+)-**8**), being also obtained on treatment of deacetylcoralloidin A (=(+)-(4*R**,8*R**,10*R**)-eudesma-5,7(11)-dien-8-ol; (+)-**2**) with $(COCl)_2$ in DMSO, is configurationally correlated to coralloidin A (=(+)-(4*R**,8*R**,10*R**)-eudesma-5,7(11)-dien-8-yl acetate; (+)-**1**). Under acidic conditions, (+)-**2** undergoes a complex rearrangement giving (+)-(3*R**,4*S**,5*R**,6*R**,7*S**)-arist-10-(1)-en -3-ol ((+)-**9**), which is also obtained, together with (+)-**8**, on attempts to mesylate (+)-**2**.

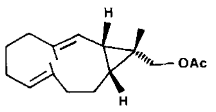
1. Introduction. – Tropical alcyonaceans are a rich source of both diterpenoids [1] [2] and sesquiterpenoids [2]. Most sesquiterpenoids are capnellanes [3], eremophilanes, neolemnanes [4], copaanes, ylanganes [5], africanes [6], aristolanes [7a], nardosinanes [7b], germacranes, and guaianes [8], though furanosesquiterpenoids have also been isolated [8]. Eudesmanes (selinanes) are rarely encountered with alcyonaceans, only a few having been isolated from either an Australian *Nephthea* sp. [9] or the Mediterranean *Alcyonium coralloides* [10]. Therefore, we report here on three new eudesmanes isolated from the latter species and to compare then with the already known coralloidin A ((+)-**1**), its deacetyl derivative (+)-**2**, and **3** [10].

2. Results and Discussion. – The extraction of *A. coralloides* (see *Exper. Part*) yielded coralloidin C ((–)-**4**), D ((–)-**7**), and E ((–)-**8**) which were identified by their spectroscopic data.

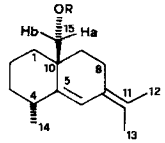
2.1. *Coralloidin C (=(–)-(4*R*,10*S*)-Eudesma-5,7(11)-dien-15-yl Acetate;* (–)-**4**). Coralloidin C is closely related to coralloidin A ((+)-**1**), previously isolated from the same animal [10]. The MS of (–)-**4** shows the molecular ion, unstable for the loss of AcOH, at the same *m/z* value (262) as the one of (+)-**1**. The ^{13}C-NMR spectra of the two compounds (*Table 1* and [10]) bear many similarities though the O-deshielded C-signal is a *t* with (–)-**4** and a *d* with (+)-**1**. At higher field, in place of the *q* of (+)-**1**, (–)-**4** shows a *t*. Thus coralloidin C ((–)-**4**) has 1 CH_3 and 1 CH group less and 2 CH_2 groups more than (+)-**1**, and the two compounds must be isomeric.



(+)-**1** R = Ac
(+)-**2** R = H



(–)-**3**



(–)-**4**[a]) R = Ac
(–)-**5**[a]) R = H
(–)-**6**[a]) R = *p*-OMe–C_6H_4CO

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[a]) Eudesmane numbering; for systematic names, see *Exper. Part.*

Table 1. *^{13}C-NMR Data*[a]) (C_6D_6, unless otherwise stated) *for Coralloidin C* ((−)-**4**), *Coralloidin D* ((−)-**7**), *Coralloidin E* ((+)-**8**), *the Derivative* (−)-**5**, *and Compound* (−)-**9**

C-Atom	(−)-**4**[b])	(−)-**5**[c])	(−)-**7**[d])	(+)-**8**	(+)-**9**	(+)-**9**[c])
C(1)	36.32 (*t*)	35.73 (*t*)	42.03 (*t*)	42.80 (*t*)	116.96 (*d*)	116.21 (*d*)
C(2)	22.29 (*t*)	22.11 (*t*)	19.30 (*t*)	22.70 (*t*)	34.89 (*t*)	34.31 (*t*)
C(3)	37.09 (*t*)	36.94 (*t*)	33.08 (*t*)	35.68 (*t*)	71.02 (*d*)	71.48 (*d*)
C(4)	34.00 (*d*)	33.79 (*d*)	133.45 (*s*)	33.20 (*d*)	40.54 (*d*)	40.12 (*d*)
C(5)	142.49 (*s*)	143.34 (*s*)	147.85 (*s*)	149.58 (*s*)	–[f])	36.30 (*s*)
C(6)	120.61 (*d*)	120.15 (*d*)	30.61 (*t*)	115.54 (*d*)	35.40 (*d*)	35.18 (*d*)
C(7)	128.20 (*s*)	127.72 (*s*)[e])	125.66 (*s*)	142.79 (*s*)	19.62 (*d*)	19.29 (*d*)
C(8)	23.01 (*t*)	22.96 (*t*)	26.83 (*t*)	114.11 (*d*)	21.39 (*t*)	21.12 (*t*)
C(9)	34.39 (*t*)	34.50 (*t*)	39.45 (*t*)	40.96 (*t*)	30.04 (*t*)	29.65 (*t*)
C(10)	39.00 (*s*)	40.28 (*s*)	34.91 (*s*)	34.87 (*s*)	144.17 (*s*)	144.64 (*s*)
C(11)	125.54 (*s*)	126.24 (*s*)[e])	120.57 (*s*)	71.44 (*s*)	18.98 (*s*)	18.93 (*s*)
C(12)	20.71 (*q*)	20.72 (*q*)	62.28 (*t*)	29.51 (*q*)[g])	15.88 (*q*)	15.59 (*q*)
C(13)	19.71 (*q*)	19.77 (*q*)	62.14 (*t*)	29.34 (*q*)[g])	30.04 (*q*)	29.93 (*q*)
C(14)	19.07 (*q*)	18.85 (*q*)	19.25 (*q*)	18.70 (*q*)	13.27 (*q*)	13.08 (*q*)
C(15)	64.81 (*t*)	65.21 (*t*)	24.47 (*q*)	22.42 (*q*)	24.89 (*q*)	24.78 (*q*)

[a]) Multiplicities from APT (see [11]).

[b]) Acetyl group: 170.17 (*s*, C=O), 20.50 (*q*, Me).

[c]) In $CDCl_3$.

[d]) Acetyl group: 170.26 and 170.22 (2*s*, C=O), 20.54 (*q*, Me).

[e])[g]) These resonances can be interchanged.

[f]) Not detected.

Table 2. *^{1}H-NMR Data* (C_6D_6, unless otherwise stated) *for Coralloidin C* ((−)-**4**), *Coralloidin D* ((−)-**7**), *Coralloidin E* ((+)-**8**), *the Derivates* (−)-**5** *and* (−)-**6**, *and Compound* (+)-**9**[a])

Protons at	(−)-**4**[b])	(−)-**5**[d])
C(1)	1.89 (br. *ddd*, J_{gem} = 12.0, *J*(1β,2β) = *J*(1β,2α) = 6.5, *J*(1β,3β) small, H_β) 1.05 (*dddd*, J_{gem} = *J*(1α,2β) = 12.0, *J*(1α,2α) = 6.0, *J*(1α,15a) = 1.2, H_α)	1.60 (H_β)[c]) 1.14 (br. *ddd*, J_{gem} = *J*(1α,2β) = 13.0, *J*(1α,2α) = 6.0, *J*(1α,15a) small, H_α)
C(2)	1.60 (*m*, H_β)[c]) 1.46 (*m*, H_α)	1.60 (H_β)[c]) 1.60 (H_α)[c])
C(3)	1.60 (*m*, H_β)[c]) 0.96 (*dddd*, J_{gem} = *J*(3α,4) = *J*(3α,2β) = 11.0, *J*(3α,2α) = 4.0, H_α)	1.79 (*m*, H_β) 1.04 (*dddd*, J_{gem} = *J*(3α,4) = *J*(3α,2β) = 12.0, *J*(3α,2α) = 5.0, H_α)
C(4)	2.06 (*m*, 1H)	2.22 (*m*, 1H)[c])
C(6)	6.33 (br. *d*, *J*(6,4) = 1.5, *J*(6,8α) small, 1H)	6.36 (br. *d*, *J*(6,4) = 2.0, *J*(6,8α) small, 1H)
C(8)	2.24 (br. *ddd*, J_{gem} = 15.6, *J*(8β,9α) = 13.2, *J*(8β,9β) = 4.2, *J*(8β,13) = 1.5, *J*(8β,12) small, H_β) 2.40 (br. *ddd*, J_{gem} = 15.6, *J*(8α,9α) = 4.5, *J*(8α,9β) = 4.2, *J*(8α,6), *J*(8α,12), and *J*(8α,13) small, H_α)	2.24 (br. *m*, H_β)[c]) 2.39 (br. *ddd*, J_{gem} = 16.0, *J*(8α,9α) = 4.5, *J*(8α,9β) = 4.2, *J*(8α,6), *J*(8α,12), and *J*(8α,13) small, H_α)
C(9)	1.98 (*ddd*, J_{gem} = 13.2, *J*(9β,8β) = *J*(9β,8α) = 4.2, H_β) 1.30 (*dddd*, J_{gem} = *J*(9α,8β) = 13.2, *J*(9α,8α) = 4.5, *J*(9α,15b) = 1.4, H_α)	1.93 (*ddd*, J_{gem} = 13.2, *J*(9β,8β) = *J*(9β,8α) = 4.2, H_β) 1.25 (*dddd*, J_{gem} = *J*(9α,8β) = 13.2, *J*(9α,8α) = 4.5, *J*(9α,15b) = 1.0, H_α)
C(12)	1.64 (br. *s*, *J*(12,8β) and *J*(12,8α) small, 3H)	1.73 (br. *s*, *J*(12,8α) small, 3H)
C(13)	1.76 (br. *d*, *J*(13,8β) = 1.5, *J*(13,8α) small, 3H)	1.82 (br. *s*, *J*(13,8α) small, 3H)
C(14)	1.02 (*d*, *J*(14,4) = 6.5, 3H)	1.09 (*d*, *J*(14,4) = 6.5, 3H)

Table 2 (cont.)

Protons at	(−)-**4**b)	(−)-**5**d)
C(15)	4.31 (*A* of *ABXY*, J_{gem} = 11.0, *J*(15b,9α) = 1.4, H$_{\mathrm{b}}$) 4.22 (*B* of *ABXY*, J_{gem} = 11.0, *J*(15a,1α) = 1.2, H$_{\mathrm{a}}$)	3.70 (*A* of *ABXY*, J_{gem} = 11.0, *J*(15b,9α) = 1.0, H$_{\mathrm{b}}$) 3.60 (*B* of *ABXY*, J_{gem} = 11.0, *J*(15a, 1α) small, H$_{\mathrm{a}}$)

Protons at	(−)-**6**c)	(−)-**7**g)
C(1)	1.99 (br. *d*, J_{gem} = 13.5, H$_{\beta}$) 1.17 (br. *ddd*, J_{gem} = *J*(1α, 2β) = 13.5, *J*(1α, 2α) = 4.0, *J*(1α, 15a) small, H$_{\alpha}$)	1.25 or 1.43 (H$_{\beta}$)c) 1.43 or 1.25 (H$_{\alpha}$)c)
C(2)	1.71 (*m*, H$_{\beta}$) 1.6 (*m*, H$_{\alpha}$)	1.40 or 1.61 (H$_{\beta}$)c) 1.61 or 1.40 (H$_{\alpha}$)c)
C(3)	1.8 (submerged, H$_{\beta}$) 1.06 (*dddd*, J_{gem} = *J*(3α, 4β) = *J*(3α, 2β) = 12.8, *J*(3α, 2α) = 4.0, H$_{\alpha}$)	1.73 or 1.88 (H$_{\beta}$)c) 1.88 or 1.73 (H$_{\alpha}$)c)
C(4)	2.29 (*m*, 1H)	–
C(6)	6.34 (br. *d*, *J*(6,4) = 1.5, *J*(6,8α) small, 1H)	2.40 (br. *d*, J_{gem} = 15.1, *J*(6β, 14) and *J*(6β, 12) small, H$_{\beta}$) 3.65 (*dd*, J_{gem} = 15.1, *J*(6α, 8α) = 1.9, H$_{\alpha}$)
C(8)	2.22 (br. *ddd*, J_{gem} = 15.3, *J*(8β, 9α) = 13,5, *J*(8β, 9β) = 4.3, *J*(8β, 12) and *J*(8β, 13) small, H$_{\beta}$) 2.44 (br. *ddd*, J_{gem} = 15.3, *J*(8α, 9β) = 4.3, *J*(8α, 9α) = 4.0, *J*(8α, 6) small, H$_{\alpha}$)	2.04 (br. *ddd*, J_{gem} = *J*(8β, 9α) = 14.5, *J*(8β, 9β) = 4.2, *J*(8β, 13) small, H$_{\beta}$) 2.50 (*dddd*, J_{gem} = 14.5, *J*(8α, 9α) = *J*(8α, 9β) = 4.4, *J*(8α, 6α) = 1.9, H$_{\alpha}$)
C(9)	2.02 (*ddd*, J_{gem} = 13.5, *J*(9β, 8β) = *J*(9β, 8α) = 4.3, H$_{\beta}$) 1.33 (*dddd*, J_{gem} = *J*(9α, 8β) = 13.5, *J*(9α, 8α) = 4.0, *J*(9α, 15b) = 1.0, H$_{\alpha}$)	1.39 (H$_{\beta}$)c) 1.23 (H$_{\alpha}$)c)
C(12)	1.74 (br. *s*, *J*(12, 8β) small, 3H)	4.82 (br. *s*, *J*(12, 6β) small, 2H)
C(13)	1.82 (br. *s*, *J*(13, 8β) small, 3H)	4.89, 4.99 (*AB* J_{gem} = 11.0, *J*(13, 8β) small, 2H)
C(14)	1.13 (*d*, *J*(14,4) = 6.8, 3H)	1.59 (br. *s*, *J*(14, 6β) small, 3H)
C(15)	4.44 (*dd*, J_{gem} = 10.5, *J*(15b, 9α) = 1.0, H$_{\mathrm{b}}$) 4.27 (br. *d*, J_{gem} = 10.5, *J*(15a, 1α) small, H$_{\mathrm{a}}$)	0.99 (*s*, 3H)

Protons at	(−)-**8**g)	(+)-**9**d)
C(1)	1.44 (H$_{\beta}$)c) 1.26 (H$_{\alpha}$)c)	5.22 (br. *dd*, *J*(1, 2α) = 5.0. *J*(1, 2β) = 2.0, *J*(1, 3) small, 1H) –
C(2)	1.56 (H$_{\beta}$)c) 1.45 (H$_{\alpha}$)c)	2.31 (br. *ddd*, J_{gem} = 18.0, *J*(2β, 3) = 4.2, *J*(2β, 1) = 2.0, H$_{\beta}$) 2.15 (br. *ddd*, J_{gem} = 18.0, *J*(2α, 1) = 5.0, *J*(2α, 3) = 2.1, H$_{\alpha}$)
C(3)	1.56 (H$_{\beta}$)c) 1.02 (*m*, H$_{\alpha}$)	3.89 (br. *ddd*, *J*(3, 2β) = 4.2, *J*(3, 2α) = *J*(3, 4) = 2.1, *J*(3β, 1) small) –
C(4)	2.10 (*m*, 1H)	1.81 (*dq*, *J*(4, 14) = 6.5, *J*(4, 3) = 2.1, 1H)
C(6)	5.98 (*dd*, *J*(6, 4) = 1.5, *J*(6, 8) = 0.9, 1H)	0.62 (*d*, *J*(6, 7) = 9.5)
C(7)	–	0.75 (*ddd*, *J*(7, 8β) = *J*(7, 6) = 9.5, *J*(7, 8α) = 3.3, 1H)
C(8)	5.58 (*ddd*, *J*(8, 9β) = 6.6, *J*(8, 9α) = 2.3, *J*(8, 6) = 0.9, 1H) –	2.02 (*dddd*, J_{gem} = 14.0, *J*(8β, 7) = 9.5, *J*(8β, 9β) = 7.4, *J*(8β, 9α) = 1.5, H$_{\beta}$) 1.45 (*dddd*, J_{gem} = 14.0, *J*(8α, 9β) = 13.0, *J*(8α, 9α) = 6.1, *J*(8α, 7) = 3.3, H$_{\alpha}$)

Table 2 (cont.)

Protons at	(−)-**8**[g])	(+)-**9**[d])
C(9)	1.94 (*dd*, $J_{\text{gem}} = 16.6$, $J(9\beta,8) = 6.6$, H_β) 2.15 (br. *dd*, $J_{\text{gem}} = 16.6$, $J(9\alpha,8) = 2.3$, $J(9\alpha,15)$ small, H_α)	2.32 (br. *ddd*, $J_{\text{gem}} = J(9\beta,8\alpha) = 13.0$, $J(9\beta,8\beta) = 7.4$, H_β) 1.78 (*ddd*, $J_{\text{gem}} = 13.0$, $J(9\alpha,8\alpha) = 6.1$, $J(9\alpha,8\beta) = 1.5$, H_α)
C(12)	1.26 or 1.29 (*s*, 3H)	1.01 (*s*, 3H)
C(13)	1.29 or 1.26 (*s*, 3H)	0.96 (*s*, 3H)
C(14)	1.09 (*d*, $J(14,4) = 6.8$, 3H)	1.16 (*d*, $J(14,4) = 6.5$, 3H)
C(15)	0.97 (br. *s*, $J(15,9\alpha)$ small, 3H)	1.28 (*s*, 3H)

Protons at	(+)-**9**
C(1)	5.11 (br. *ddd*, $J(1,2\alpha) = 5.0$, $J(1,2\beta) = J(1,9\beta) = 1.8$, $J(1,3)$ small, 1H)
C(2)	2.09 (*dddd*, $J_{\text{gem}} = 18.0$, $J(2\beta,3) = 4.8$, $J(2\beta,9\beta) = 2.5$, $J(2\beta,1) = 1.8$, H_β) 1.92 (*dddd*, $J_{\text{gem}} = 18.0$, $J(2\alpha,1) = 5.0$, $J(2\alpha,3) = 2.8$, $J(2\alpha,9\beta) = 2.5$, H_α)
C(3)	3.62 (br. *ddd*, $J(3,2\beta) = 4.8$, $J(3,2\alpha) = 2.8$, $J(3,4) = 2.5$, $J(3\beta,1)$ small, 1H)
C(4)	1.70 (*dq*, $J(4,14) = 6.7$, $J(4,3) = 2.5$, 1H)
C(6)	0.57 (*d*, $J(6,7) = 9.3$)
C(7)	0.68 (*ddd*, $J(7,8\beta) = J(7,6) = 9.3$, $J(7,8\alpha) = 3.3$, 1H)
C(8)	1.93 (*dddd*, $J_{\text{gem}} = 14.0$, $J(8\beta,7) = 9.3$, $J(8\beta,9\beta) = 7.0$, $J(8\beta,9\alpha) = 1.5$, H_β) 1.46 (*dddd*, $J_{\text{gem}} = 14.0$, $J(8\alpha,9\beta) = 13.5$, $J(8\alpha,9\alpha) = 6.0$, $J(8\alpha,7) = 3.3$, H_α)
C(9)	2.32 (*dddddd*, $J_{\text{gem}} = J(9\beta,8\alpha) = 13.5$, $J(9\beta,8\beta) = 7.0$, $J(9\beta,2\beta) = J(9\beta,2\alpha) = 2.5$, $J(9\beta,1) = 1.8$, H_β) 1.72 (*ddd*, $J_{\text{gem}} = 13.5$, $J(9\alpha,8\alpha) = 6.0$, $J(9\alpha,8\beta) = 1.5$, H_α)
C(12)	1.02 (*s*, 3H)
C(13)	0.96 (*s*, 3H)
C(14)	1.13 (*d*, $J(14,4) = 6.7$, 3H)
C(15)	1.41 (*s*, 3H)

[a]) The notation 'small' indicates sharpening of the signal on double irradiation which implies coupling constants smaller than 0.5 Hz. Coupling constants are derived from double-resonance experiments.

[b]) Acetyl group: 1.69 (*s*).

[c]) Superimposed.

[d]) In $CDCl_3$.

[e]) Aromatic group: 3.85 (*s*, MeO); 6.92, 7.99 (*AB*, C_6H_4).

[f]) Acetyl groups: 1.67 (*s*) and 1.69 (*s*).

[g]) Assignment from one-bond $^{13}C,^{1}H$ shift correlation [12].

In the ^1H-NMR spectrum[1]) of (−)-**4** *(Table 2)*, the *ABX* system due to $CH_2(9)$ and H–C(8) of (+)-**1** [10] is replaced by a set of signals attributable to the isolated $CH_2(8)$–$CH_2(9)$ system. There is also evidence that the $CH_3(15)$ *s* of (+)-**1** is replaced in (−)-**4** by an *AB* system for a CH_2 group[2]), further splitted (see below) by coupling with H_α–C(1) and H_α–C(9) *(Table 2)*. On the other hand, (−)-**4** (*Table 2* and UV) preserves the *d* of $CH_3(14)$, the isopropylidene group, and the conjugated diene system of (+)-**1** [10]. The couplings of H–C(6) with both H_α–C(8) and H–C(4), of H–C(4) with H_α–C(3), and of $CH_2(1)$ with $CH_2(2)$ lead to structure (−)-**4**.

^1H-NMR experiments with the deacetylated product (−)-**5** in the presence of $Eu(fod)_3$ (molar ratio substrate/$Eu(fod)_3$ 2:1) support the relative configuations at C(10) and C(4). In fact, H–C(4) undergoes a low-field shift ($\Delta\delta$ 1.1 ppm) twice as large as $CH_3(14)$ ($\Delta\delta$ 0.5 ppm).

The ^1H-NMR spectra of deacetylcoralloidin C *p*-anisate ((−)-**6**) *(Table 2)* show that there are W relationships between H_a–C(15) and H_α–C(1) and between H_b–C(15) and H_α–C(9). This must reflect the importance of conformer (−)-**6** where H_b lies in a plane with C(15)–C(10)–C(9)–H_α while H_a lies in a plane with C(15)–C(10)–C(1)–H_α. This is

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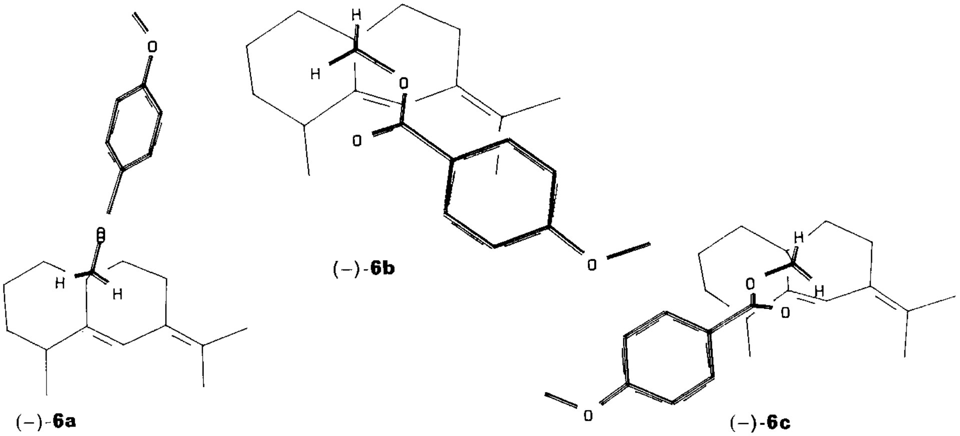
[1]) The assignment of all H-bearing C-atoms are supported by one-bond ^{13}C, ^1H shift correlation data [12].

[2]) The typical low-field shift (4.31 and 4.22 (C*H*$_2$), 64.81 ppm (*C*H_2)) indicates its attachment to the AcO group.

relevant as to the absolute configuration of (−)-**6**. Thus its CD spectra (*Exper. Part*) reveal a positive and a negative *Cotton* effect at longer and shorter wavelength, respectively, which means, according to the exciton-coupling theory [13], that (−)-**6** (and (−)-**4**) represent the absolute configuration.

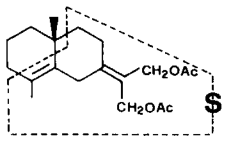
The latter problem can be further discussed on the basis of molecular-mechanics calculations [14] which leave under examination the three conformers (−)-**6a**, (−)-**6b**, and (−)-**6c** only (*Fig.*). Conformer (−)-**6a** alone is held responsible for the observed exciton coupling, since with conformer (−)-**6b**, the two chromophores make a dihedral angle of *ca.* 0° [13], whereas conformer (−)-**6c** is of higher strain energy [14].



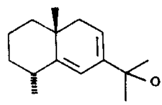
(−)-**6a** (−)-**6b** (−)-**6c**

Fig. *View from above the mean plane of the bicyclic system of the preferred conformers from MMPMI calculations* [14] *of deacetylcoralloidin-C* p-*anisate* ((−)-**6**)

2.2. *Coralloidin D* (=(−)-(*10* R*)*-Eudesma-4,7(11)-diene-12,13-diyl Diacetate* (−)-**7**). Subtracting the signals for two AcO groups, the ^{13}C-NMR spectrum of coralloidin D ((−)-**7**; *Table 1*) shows 15 resonances as for a sesquiterpenoid. This spectrum laks the isopropylidene *q* of both coralloidin A ((+)-**1**) and coralloidin C ((−)-**4**), but the other ^{13}C-NMR signals are quite similar. Moreover, the ^{1}H-NMR spectrum (*Table 2*) of (−)-**7** shows a *s* for a CH_3 group at a double bond instead of the *d* of either (+)-**1** or (−)-**4**. This suggests an eudesmane structure for (−)-**7** which, owing to tetrasubstitution at the two olefinic, non-conjugated bonds (*Table 1* and UV spectra) must be



(−)-**7**



(+)-**8**

represented by structure (−)-**7**. These conclusions are confirmed by further ^{1}H-NMR data: The signals of $CH_2(6)$ and $CH_2(8)$, apart from geminal coupling within each group, can be interpreted in terms of the H_α–C(6) *dd* arising from a W relationship with H_α–C(8) and the H_β–C(6) br. *d* arising from long-range couplings with both $CH_3(14)$ and $CH_2(12)$. In addition, the fact that H_β–C(8) appears as a br. *ddd* suggests coupling with a vicinal CH_2 group (which is confirmed by double-irradiation experiments) and homoallylic coupling with $CH_2(13)$. The thus derived partial structure S for (−)-**7** is in accordance with the fact that the signals for $CH_2(9)$ are submerged by the other signals, in contrast to the situation in (+)-**1** and (−)-**4**. Moreover, the assignment of the AcOCH_2 groups is fully supported by NOE differential positive effects[3]) and double-resonance experiments show that the $CH_2(8)$–$CH_2(9)$ system is spin isolated[4]).

2.3. *Coralloidin E (=(+)-(4*R**, 10*R**)-Eudesma-5,7-dien-11-ol;* (+)-**8**). Mass and ^{13}C-NMR spectra of (+)-**8** indicate the same number of skeletal C-atoms, double bonds, and cycles as for coralloidin A ((+)-**1**), C ((–)-**4**), and D ((–)-**7**), whilst there is no AcO group *(Table 1)*. The 2 double bonds of (+)-**8** do not bear any CH_3 group, in contrast with the other coralloidins. Moreover, the fact that the UV absorption of (+)-**8** is shifted to longer wavelength and is weaker than the one of both (+)-**1** and (–)-**4** suggests homoannular conjugation. Of the 4 CH_3 groups of (+)-**8**, one is a *d* in the ^1H-NMR spectrum *(Table 2)*, like $CH_3(14)$ of both (+)-**1** and (–)-**4**, whilst 2 other CH_3 groups are deshielded, apparently by 1 OH group. Imagining that the isopropylidene group of (+)-**1** and (–)-**4**, or the substituted isopropylidene group of (–)-**7** has been changed into a 2-hydroxyisopropyl group (which is suggested by the ^{13}C-NMR *s* at 71.44 ppm (*s*)), an eudesmane structure is an attractive hypothesis also for (+)-**8**. Like H–C(6) of (+)-**1** or (–)-**4**, one olefinic C*H* of (+)-**8** bears only long-range couplings, whilst the other must be bound to a CH_2 group. The one-bond ^{13}C, ^1H shift correlations [12], and ^1H-NMR double-resonance experiments are in accordance with structure (+)-**8**, the latter revealing the couplings $CH_3(14)$, H–C(4), H–C(4), H–C(6), H–C(6), H–C(8), H–C(8), H_α–C(9), H–C(8), H_β–C(9), and H_α–C(9), $CH_3(15)$. The remaining 3 CH_2 groups (assignments based on ^{13}C, ^1H shift correlations) could not be spin-correlated. However, the ^{13}C-NMR data (see above) and biogenetic reasons suggest that they are placed between C(10) and C(4). This is fully confirmed by the chemical transformation of (+)-**2** into (+)-**8** as discussed below.

2.4. *Attempts at Determining the Absolute Configuration of Coralloidin A* ((+)-**1**). *Horeau's Method.* The results *(Exper. Part)* of the application of *Horeau*'s method [15] to deacetylcoralloidin A ((+)-**2**) are such that, should the angular CH_3 group be selected as the larger group, (+)-**2** would be represented by the mirror image of the structure given above. If so, coralloidin A would have opposite absolute configuration to coralloidin C ((–)-**4**), as derived from CD spectra [13] of (–)-**6**. This is unlikely for closely related terpenoids isolated from the same animal.

This conflict can be reconciled if the reacting conformer of (+)-**2** in *Horeau*'s esterification [15] has the OH group in the equatorial position. The isopropylidene group can thus be taken as the bulkier group, and the absolute configuration is represented by structure (+)-**2**.

Attempts at Epimerizing (+)-**2**. To prove directly the latter point, we have unsuccessfully attempted to epimerize (+)-**2** at C(8). *Corey*'s method involving KO_2 treatment of the mesylate [16] could not be applied as, under typical conditions for mesylation, (+)-**2** gave a 1:1 mixture of coralloidin E ((+)-**8**) and the aristolane sesquiterpenoid (+)-**9**[5]) besides 45% of unreacted (+)-**2** *(Scheme)*. Also HCOOH and Ph_3P in the presence of diethyl azodicarboxylate [17] failed to give the desired epimer, (+)-**9** being obtained

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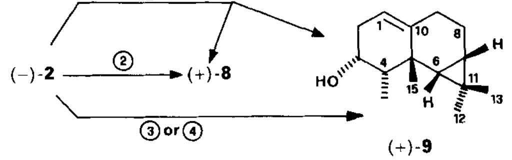
[3]) On irradiation of (–)-**7** in C_6D_6 at 3.65 ppm (H_α–C(6)), the following signal increases were observed: 21% at 2.40 (H_β–C(6)), 6% at the *AB* pattern ($CH_2(13)$), and 4% at 1.59 ppm ($CH_3(14)$). On irradiation at either 1.59 ($CH_3(14)$) or *ca.* 4.95 ppm ($CH_2(13)$), a 7 or 3.3% increase, respectively, at 3.65 ppm (H_α–C(6)) was observed. Finally, on irradiation at 4.82 ppm ($CH_2(12)$), there was a 12% increase at 2.50 ppm (H_α–C(8)).

[4]) On irradiation of (–)-**7** in $CDCl_3$ at 2.26 ppm (H_β–C(8)), 2 *dd* emerged at 1.58 and 1.26 ppm (each with $J = 12.5, 4.2$). On irradiation at 2.53 ppm (H_α–C(8)), 2 *dd*, emerged at 1.58 ($J = 12.5, 4.0$) and 1.26 ppm ($J = 12.5, 12.5$).

[5]) Structure (+)-**9** is based on ^{13}C- *(Table 1)* and ^1H-NMR data *(Table 2)* and on the MS *(Exper. Part)*. These data clearly indicate the three-membered ring, and support directly all the connectivities of structure (+)-**9**, except those of C(5) with its adjacent C-atoms, and, obviously, the locations of the CH_3 groups (*s* in the ^1H-NMR). However, the structure of (+)-**9** was confirmed by the following differential, positive NOE effects in the ^1H-NMR (C_6D_6): irradiation at 0.57→3% on both 0.96 and 1.41 and 2% on 1.13, at 0.96→3% on 0.57, at 1.02→19% on 1.46, at 1.13→6% on 0.57, at 1.41→11 and 6% on 2.32 and 0.57, resp., at 2.32→4% on 1.41 ppm.

Scheme



① $MeSO_2Cl$, Et_3N, CH_2Cl_2, –20°.
② $(COCl)_2$, DMSO.
③ HCO_2H, Ph_3P, diethyl azodicarboxylate.
④ HCl or long standing in $CDCl_3$.

instead[6]. Similarly, (+)-**9** was formed from (+)-**2** either on treatment with aq. HCl or on long standing in $CDCl_3$ solution (NMR).

Formation of (+)-**8** can be merely the result of allylic rearrangements of carbonium ions, whilst the remote refunctionalization of (+)-**2** with formation of (+)-**9** is a more interesting phenomenon which requires an array of unusual hydride shifts. Coralloidin E ((+)-**8**) can not be an intermediate of the latter transformation as it fails to form (+)-**9** on treatment with HCl. ^1H-NMR spectra for the product of this transformation, obtained directly from the reaction mixture, are in accordance with the structure of eudesma-3,5,7(11)-triene [18].

We thank Mr. *J. Mabit* and Mr. *G. Boyer* for much help in collecting the animal, Dr. *S. Weinberg* for the identification, the *Laboratoire Arago* for laboratory facilities, and the *Provincia Autonoma di Trento*, the *C.N.R.*, and the *M.P.I.* (Progetti di Interesse Nazionale), Roma, for financial support.

Experimental Part

1. *General.* All evaporations were carried out at reduced pressure. Column chromatography: *Merck* silica gel *60*, 63–200 µm. TLC: *Merck-60-254* silica-gel plates. HPLC: *Merck-LiChrosorb-Si-60* (7 µm) or *Merck-LiChrosorb RP8 or RP18* (7 µm; reverse phase), 25 × 1-cm columns, 5 ml eluent/min. Polarimetric data: *JASCO-DP-181* digital polarimeter. UV (λ_{max} in nm, ε in mol^{-1} l cm^{-1}): *Perkin-Elmer-Lambda-3*. IR (ν_{max} in cm^{-1}): *Pye-Unicam SP3 200S*. 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. EI-MS (*m/z* (%)): home-built spectrometer based on the *ELFS-4-162-8-Extranuclear* quadrupole [19]. MMPMI calculations include pi calculations (the planar pi geometry is best accepted) with neither atom restrictions nor added constants.

2. *Isolations. A. coralloides*, collected in July–August 1985 in French East Pyrenean Mediterranean waters [20], was extracted with EtOH, the EtOH evaporated, and the residue extracted with petroleum ether [10]. After evaporation the residue (18 g) was column chromatographed on 450 g of support with a gradient of petroleum ether/Et_2O. Coralloidin C ((–)-**4**) was eluted with petroleum ether/Et_2O 9:1 and coralloidin D ((–)-**7**) and coralloidin E ((+)-**8**) with petroleum ether/Et_2O 4:6. HPLC purification of (–)-**4**: hexane/THF 99:1, t_R 11 min; 0.031 g (0.17% of the petroleum-ether extract). HPLC separation of (–)-**7** and (+)-**8**: *RP18*, MeOH/H_2O 7:3, t_R 29 min (0.015 g, 0.08%) and 25.5 min (0.008 g, 0.04%), resp.

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[6] Even an attempt to circumvent the problem *via* oxidation of (+)-**2** with $(COCl)_2$DMSO to the corresponding ketone followed by reduction with inversion of configuration was met with failure. In fact, (+)-**8** was recovered from the attempted oxidation.

3. *Coralloidin C* (*= (–)-(1*R*,4a*S*)-1,2,3,4,4a,5,6,7-Octahydro-1-methyl-7-isopropylidenenaphthalene-4a-methyl Acetate;* (–)-**4**). Colourless oil. $[\alpha]_D^{20} = -168.7°$ ($c = 0.34$, $CHCl_3$). UV (EtOH): 249 (16000). MS: 262 (4, $M^{+\cdot}$), 202 (15, $M^{+\cdot}$ – AcOH), 190 (12), 189 (100), 187 (42), 159 (19), 147 (14), 145 (16), 133 (19), 131 (23), 119 (14), 117 (8), 107 (11), 105 (8), 93 (8), 91 (21), 82 (9), 55 (15), 43 (15).

4. *Deacetylcoralloidin C* (*= (–)-1,2,3,4,4a,5,6,7-Octahydro-1-methyl-7-isopropylidenenaphthalene-4a-methanol;* (–)-**5**). For 30 min, (–)-**4** (6 mg, 0.023 mmol) was heated at reflux in 4% KOH/MeOH. The mixture was extracted with hexane/Et_2O 1:1 the org. phase evaporated, and the residue subjected to HPLC (hexane/isopropyl ether 1:1) 3.5 mg (70%) of (–)-**5**, t_R 15.5 min. $[\alpha]_D^{20} = -172.9°$ ($c = 0.14$, EtOH). UV (EtOH): 250.0 (15000). MS: 220 (8, $M^{+\cdot}$), 202 (7, $M^{+\cdot} - H_2O$), 190 (16), 189 (100), 187 (9), 147 (8), 145 (7), 131 (11), 119 (8), 117 (7), 105 (11), 91 (20).

5. *Deacetylcoralloidin C* p-*Anisate* (*= (–)-1,2,3,4,4a,5,6,7-Octahydro-1-methyl-7-isopropylidenenaphthalene-4a-methyl* p-*Methoxybenzoate;* (–)-**6**). To (–)-**5** (2 mg, 0.0091 mmol) in 2 drops of dry pyridine, *p*-methoxybenzoyl chloride was added. After *ca.* 12 h, the mixture was extracted with petroleum ether, the org. layer evaporated, and the residue subjected to HPLC (hexane/isopropyl ether 1:1): 2.2 mg (95% on reacted (–)-**5**) of (–)-**6**. Colourless oil. $[\alpha]_D^{20} = -55.0°$ ($c = 0.04$, EtOH). UV (EtOH): 204.0 (53000), 252.0 (39000). CD (EtOH, $2.77 \cdot 10^{-5}$ M; cell, optical path 1 cm; sensitivity 2; λ in nm (elongation in cm, $\Delta\varepsilon$ in $mol^{-1} l cm^{-1}$, $\Delta\varepsilon/\varepsilon$)): 243 (–8.8, –19.3, $-7.9 \cdot 10^{-2}$), 265 (+6.6, +14.4, $+5.45 \cdot 10^{-2}$).

6. *Coralloidin D* (*= (–)-(4a*R**)-2-[3,4,4a,5,6,7-Hexahydro-4a,8-dimethylnaphth-2(1*H*)-ylidene]propane-1,3-diyl Diacetate;* (–)-**7**). Colourless oil. $[\alpha]_D^{20} = -14.1°$ ($c = 0.227$, EtOH). UV (EtOH): 208.0 (10000). MS: 260 (69, $M^{+\cdot}$ – AcOH), 202 (24), 200 (58, 260 – AcOH), 187 (37), 186 (15), 185 (100, $M^{+\cdot}$ – 60 – Me), 171 (17), 159 (30), 157 (34), 145 (48), 143 (50), 141 (15), 131 (44), 128 (15), 117 (21), 105 (25), 91 (23), 43 (33).

7. *Coralloidin E* (*= (–)-(4a*R*,*8*R**)-2-[4,4a,5,6,7,8-Hexahydro-4a,8-dimethylnaphth-2-yl]propan-2-ol;* (+)-**8**). Crystals, m.p. 55°. $[\alpha]_D^{20} = +305.0°$ ($c = 0.09$, EtOH). UV (EtOH): 263 (8400). MS: 220 (0.1, $M^{+\cdot}$), 205 (3, $M^{+\cdot}$ – 15), 202 (37, $M^{+\cdot} - H_2O$), 187 (100, $M^{+\cdot} - H_2O$ – Me), 159 (14), 145 (44), 132 (17), 131 (81), 129 (10), 128 (10), 105 (16), 91 (16).

8. Horeau*'s Procedure with (+)-***2**. To deacetylcoralloidin A ((+)-**2**) [10] (26.5 mg, 0.12 mmol) in 1.34 ml of dry pyridine was added (±)-α-phenylbutyric anhydride (93 mg), and the mixture was stirred for 4 h at r.t. Then, H_2O (0.3 ml) was added, the mixture stirred for 1 h, titrated with 0.1M NaOH, and extracted with Et_2O. The aq. residue was acidified and then extracted with Et_2O obtaining α-phenylbutyric acid with $\alpha_D = +0.025°$ (10-cm optical path cell, 5 ml of C_6H_6). Esterification: 40% yield. Optical yield: 16.4%.

9. *Attempted Epimerization of Deacetylcoralloidin A* ((+)-**2**). 9.1.Via *Mesylate* [16]. A mixture of (+)-**2** [10] (8 mg), $MeSO_2Cl$, and Et_3N (2 mol-equiv. each) in CH_2Cl_2 was left at –20° C for 1 h and then evaporated. The residue gave, after TLC (silica-gel, petroleum ether/Et_2O 95:5), (+)-**8** (14%), aristolane ((+)-**9**, 14%), and unreacted (+)-**2** (45%).

9.2. *Treatment with Diethyl Azodicarboxylate/Triphenylphosphine* [17]. To a mixture of (+)-**2** (12 mg), PPh_3, and HCO_2H (2 mol-equiv. each) in 3 ml of dry THF was added 0.1 ml of THF containing 2 mol-equiv. of diethyl azodicarboxylate. The mixture was stirred overnight at r.t. Evaporation and TLC of the residue with petroleum ether/Et_2O 9:1, followed by HPLC (*RP8* CH_3CN/H_2O 65:35, t_R 9.9 min), afforded aristolane (+)-**9** (30%).

9.3. Via *Oxidation to Ketone* [21]. Working at –60° with dry reagents under N_2, oxalyl chloride (0.0028 ml, 0.032 mmol) in 3 ml of CH_2Cl_2 was mixed to DMSO (0.0047 ml, 0.066 mmol) in 0.05 ml of CH_2Cl_2. After 10 min, (+)-**2** (7 mg, 0.032 mmol) was added, followed, after 45 min, by Et_3N (0.4 ml). The mixture was allowed to reach r.t., H_2O added, and the org. layer separated and evaporated. The residue was subjected to HPLC (hexane/THF 95:5): 3.5 mg (50%) of (+)-**8**, t_R 17.5 min.

*Data of (+)-(3*R*,*4*S*,*5*R*,*6*R*,*7*S**)-Arist-10(1)-en-3-ol (= (+)-(1a*R*,*6*S*,*7*R*,*7a*S*,*7b*S**)-1a,2,3,5,6,7,7a,7b-Octahydro-1,1,7,7a-tetramethyl-1*H*-cyclopropa*[a]*naphthalen-6-ol;* (+)-**9**). Colourless oil. $[\alpha]^{20°} = +53.75$ (365), +18.75 (546), +13.75 (589) ($c = 0.08$, EtOH). MS: 220 (1, $M^{+\cdot}$), 202 (0.5, $M^{+\cdot} - H_2O$), 187 (11, $M^{+\cdot} - H_2O$ – Me), 178 (8), 177 (100, $M^{+\cdot} - C_3H_7$), 161 (8), 159 (43, 177 – H_2O), 149 (5), 145 (12), 133 (11), 131 (12), 119 (17), 107 (7), 105 (21), 93 (8), 91 (16), 79 (9), 69 (6).

10. *Acidic Treatment of (+)-***8**. N_2 was bubbled, in the order, through aq. 35% HCl soln. and a $CDCl_3$ soln. of (+)-**8** in the NMR tube. ^1H-NMR (direct observation): 6.36 (*s*, 1H); 5.61 (1 *m*, $w_{1/2} = 10.5$, 1H); 1.85, 1.84, 1.78 (3 br. *s*, each 3H); 0.97 (*s*, 3H); 2.52 (br. *d*, $J_{gem} = 15$, 1H) [18].

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