30. Isolation of the Cembranoid Preverecynarmin Alongside Some Briaranes, the Verecynarmins, from Both the Nudibranch Mollusc *Armina maculata* and the Octocoral *Veretillum cynomorium* of the East Pyrenean Mediterranean Sea[1])

by **Antonio Guerriero, Michele D'Ambrosio,** and **Francesco Pietra***

Istituto di Chimica, Università di Trento, I–38050 Povo-Trento

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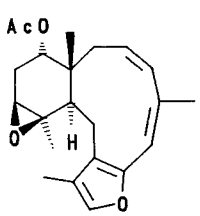
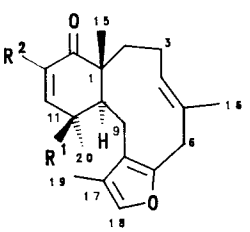
It is shown that the nudibranch mollusc *Armina maculata* and its prey, the pennatulacean octocoral *Veretillum cynomorium*, of east Pyrenean waters contain a novel cembranoid, preverecynarmin ((+)-**8**), besides the known cembranoid cembrene C (**9**) and three further briarane diterpenoids (verecynarmin E ((−)-**5**), F ((−)-**6**), and G ((−)-**7**)). A biogenetic scheme is proposed.

1. Introduction. – We have recently isolated the briarane diterpenoids verecynarmin A ((−)-**1**) [1a], B ((−)-**2**), C ((−)-**3**), and D ((−)-**4**) [1b] from both the nudibranch mollusc *Armina maculata* and its prey, the pennatulacean coral *Veretillum cynomorium*. Although nudibranchs are well known for accumulating dietary products [2], these are the first examples of briaranes from a marine mollusc.

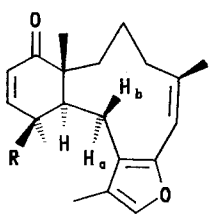
In continuation of these studies, we have now isolated from the above species three further briaranes besides two cembranoids. These are the first examples of cembranoids from a pennatulacean coral[2]).



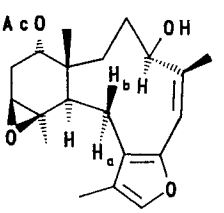
(−)-**1**



(−)-**2** $R^1 = R^2 = H$
(−)-**3** $R^1 = OH$, $R^2 = H$
(−)-**4** $R^1 = OH$, $R^2 = Cl$



(−)-**5** R = OH
(−)-**6** R = H



(−)-**7**

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

[2]) Up to now, the only known source of cembranoids from Mediterranean marine organisms was the alcyonacean *Alcyonium (= Parerythropodium) coralloides* [3].

2. Results and Discussion. – 2.1. *The Briaranes.* All novel briaranes described here were isolated from *A. maculata* but could also be detected by HPLC in *V. cynomorium.* One of these compounds, called verecynarmin E ((–)-**5**), has MS *(Exper. Part)* and ^{13}C-NMR spectra *(Table)* quite similar to those of verecynarmin C ((–)-**3**); this is true also with regard to conformational phenomena [1b] although the coalescence temperature is lower[3]). The structure of (–)-**5** is established by a detailed comparison of the data of (–)-**5** and (–)-**3**.

Table. *^{13}C-NMR Data* (C_6D_6) *of Verecynarmin E* ((–)-**5**), *Verecynarmin F* ((–)-**6**), *Verecynarmin G* ((–)-**7**), *and Preverecynarmin* ((+)-**8**)[a])

C-Atom	(–)-**5** (54.7°)[b])	(–)-**6** (45.5°)[c])	(–)-**7** (55°)[d])	(+)-**8**
C(1)	50.96 (*s*)	50.94 (*s*)	38.74 (*s*)	146.85 (*s*)
C(2)	37.74 (br. *t*)	–	39.55 (br. *t*)	119.03 (*d*)
C(3)	23.16 (*t*)	26.19 (*t*)	30.48 (br. *t*)	125.99 (*d*)
C(4)	34.58 (*t*)	34.52 (*t*)	71.10 (br. *d*)	139.87 (*s*)
C(5)	142.78 (*s*)	142.71 (*s*)	142.21 (*s*)	46.14 (*t*)
C(6)	116.98 (*d*)	116.86 (*d*)	118.40 (*d*)	70.24 (*d*)
C(7)	149.00 (*s*)	149.04 (*s*)	148.28 (*s*)	124.47 (*d*)
C(8)	119.81 (br. *s*)	–	123.52 (br. *s*)	129.99 (*s*)
C(9)	19.91 (*t*)	19.78 (*t*)	23.06 (*t*)	39.45 (*t*)
C(10)	40.02 (br. *d*)	–	–	24.84 (*t*)
C(11)	69.28 (*s*)	37.57 (*d*)	62.55 (*s*)	124.09 (*d*)
C(12)	151.47 (*d*)	153.60 (*d*)	60.12 (*d*)	134.31 (*s*)
C(13)	126.70 (*d*)	127.05 (*d*)	27.71 (*t*)	36.96 (*t*)
C(14)	203.03 (*s*)	202.19 (*s*)	79.50 (*d*)	27.99 (*t*)
C(15)	22.26 (*q*)	22.78 (*q*)	17.90 (br. *q*)	32.96 (*d*)
C(16)	22.73 (*q*)	22.87 (*q*)	16.41 (*q*)	21.93 (*q*)
C(17)	121.43 (*s*)	120.80 (*s*)	121.64 (*s*)	23.01 (*q*)
C(18)	137.77 (*d*)	137.70 (*d*)	138.13 (*d*)	17.15 (*q*)
C(19)	8.73 (*q*)	8.65 (*q*)	8.56 (*q*)	16.45 (*q*)
C(20)	30.61 (*q*)	18.59 (*q*)	23.39 (*q*)	18.15 (*q*)
CH_3CO			169.19 (*s*)	169.59 (*s*)
CH_3CO			20.56 (*q*)	21.04 (*q*)

[a]) A dash stands for 'not detected'; the assignment of H-bearing C-atoms are based on one-bond ^{1}H,^{13}C heterocorrelations [11].

[b]) The assignment of not-H-bearing C-atoms were made by comparison with (–)-**3**.

[c]) The assignment of not-H-bearing C-atoms were made by comparison with (–)-**2** and (–)-**5**.

[d]) The assignment of not-H-bearing C-atoms were made by comparison with (–)-**1** and (–)-**5**.

As concerns ^{1}H-NMR spectra, (–)-**5** lacks diallylic CH_2 signals, whereas a br. *q* for an olefinic proton replaces the br. *dd* of (–)-**3**; otherwise, the ^{1}H-NMR data are very similar. This and the fact that broadening of the above *q* arises from long-range coupling with H_a–C(9) suggest the C(5)=C(6) position for the olefinic bond in (–)-**5**. This is confirmed by UV data (λ_{max} 264 nm) which indicate conjugation of the olefinic bond with the furan ring. Contrary

[3]) In fact, at 22°, all C-atoms except C(1) and all protons of the ten-membered cycle of verecynarmin E ((–)-**5**) give broad resonances which become less broad on raising the temperature to 55°; however, even under these conditions, ^{1}H,^{1}H-coupling constants among 2 H–C(2), 2 H–C(3), and 2 H–C(4) could not be deduced; such connectivities were derived from ^{1}H,^{1}H COSY experiments *(Exper. Part)*.

to the case of (−)-**3**, the olefinic bond in (−)-**5** has no shielding effect on either H_a–C(9), H_b–C(9), or H–C(10), as revealed by the relatively low-field resonance for these protons. This implies that these two verecynarmins differ considerably in the spatial arrangement of the ten-membered ring, which does not only depend on the different position, but also on the different configuration of the olefinic bond in the two compounds. It has (*E*)-configuration in (−)-**3** [1b], whereas a relatively low-field ^{13}C(16) resonance (22.73 ppm) suggests (*Z*)-configuration in (−)-**5**. As a consequence, CH_2(3) in (−)-**5**, being subjected to steric compression by Me(15) and Me(16), resonates at relatively high field (23.16 ppm).

Another novel compound isolated from *A. maculata*, verecynarmin F ((−)-**6**), shows MS *(Exper. Part)* and ^{13}C-NMR spectra *(Table)* quite similar to those of verecynarmin B ((−)-**2**). Elucidation of the structure of this new briarane is based on similar arguments as for the couple (−)-**5** and (−)-**3**, though less detailed spectral data are available for (−)-**6** because of the meager amount of compound at hand and the intervention of conformational phenomena (no detection of C(2), C(8), and C(10) in the ^{13}C-NMR even not at 45.5°). The conclusion is that (−)-**6** is simply an isomer of (−)-**2** with a shift in position and different configuration of the olefinic bond. However, it can be ruled out that verecynarmin E ((−)-**5**) and F ((−)-**6**) are artifacts of isomerization of verecynarmin C ((−)-**3**) and B ((−)-**2**), respectively, during workup: in a blank experiment, neither (−)-**3** nor (−)-**2** underwent any change under the extraction/workup conditions during 45 h in the presence of silica gel.

Yet another novel compound isolated from *A. maculata*, verecynarmin G ((−)-**7**), is suggested to be a briarane from its NMR spectra (*Table* and *Exper. Part*) which resemble those for verecynarmin A ((−)-**1**) with regard to the epoxycyclohexane part. Further comparison with verecynarmin E ((−)-**5**) establishes its structure.

A close match of the NMR signals of (−)-**7** and (−)-**5** with regard to the C(6)-to-C(10) portion (including the methylfuran moiety and also as far as slow conformational changes are concerned) is observed, whereas a CH-heteroatom group must have replaced a CH_2 group in the C(1)-to-C(5) part. The MS *(Exper. Part)* of (−)-**7** matches that of verecynarmin A ((−)-**1**) in the region below $[M - H_2O]^+$, which suggests that verecynarmin G ((−)-**7**) is a hydrated form of (−)-**1**; this allows us to assign δ(C) at 71.10 (*d*) and δ(H) at 4.55 ppm (br. *t*) to a CHOH group. These observations and a CH_2CH_2CH moiety derived from ^{1}H,^{1}H COSY experiments which is extended to $CH_2CH_2CHC(CH_3)$=CH from both delayed ^{1}H,^{1}H COSY and decoupling experiments fully support structure (−)-**7**. The configuration rests on the similarity of the ^{13}C-NMR spectra with those of both (−)-**5** and (−)-**6** with regard to the C(5)-to-C(9) portion, including the methylfuran moiety. The configuration at C(6) is based on both a large (6.4 ppm) γ-gauche effect of OH on C(16) and a relatively low-field ^{1}H-NMR resonance for Me(16) (1.78 ppm) which implies a close proximity of OH to Me–C(16).

2.2. *The Cembranoids.* Another compound isolated from both *A. maculata* and *V. cynomorium*, called preverecynarmin ((+)-**8**), fails to show the spectral characteristics of briarane diterpenoids. Its composition $C_{22}H_{34}O_2$ is derived from both the mass spectrum (M^+ at *m/z* 330; *Exper. Part*) and the ^{13}C-NMR spectrum *(Table)* and its cembranoid structure assigned on grounds of further spectral data.

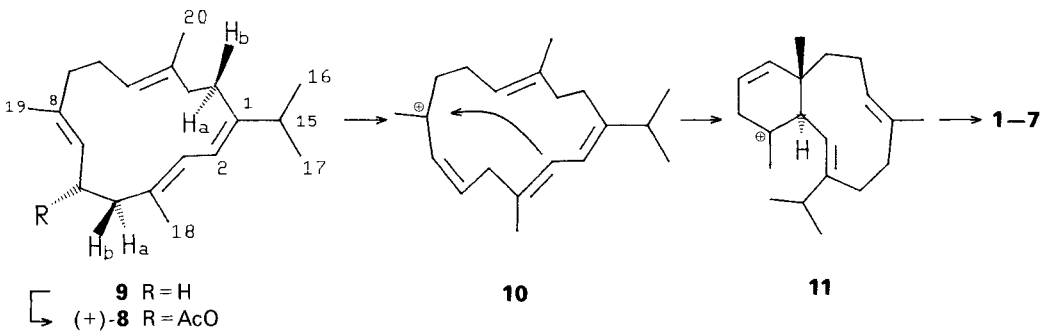
The ^{13}C-NMR spectrum of (+)-**8** reveals 22 signals for 6 Me, 5 CH_2, 1 aliphatic CH, 1 aliphatic CH bound to heteroatom, 4 olefinic CH, 4 olefinic disubstituted C, and 1 ester C=O. Its ^{1}H-NMR spectrum *(Exper. Part)* defines the ester group as an AcO group, thus suggesting a diterpenoid which, to account for the presence of 4 double bonds, must be monocyclic. In addition, three ^{13}C-NMR resonances at < 20 ppm suggest that 3 Me groups are at trisubstituted olefinic bonds in the (*E*)-configuration; the remaining 2 Me groups must be part of an i-Pr group at an olefinic bond in order to account for the low-field ^{1}H-NMR signal at 2.25 ppm *(sept.)*. These data are compatible with a cembranoid structure bearing an AcO substituent. The ^{1}H-NMR signals at 2.05–2.65 ppm *(Exper. Part)* indicate that all CH_2 groups are of the allylic type. Moreover, there must be conjugation between 2 of the 4 olefinic bonds in order to account for a UV absorption at λ_{max} 251 nm and a $J \approx 11$ between the 'internal'

protons of the diene fragment[4]). These data and a 5% NOE enhancement at H–C(15) resulting from irradiation at H–C(2) support structure (+)-**8**. Only the AcO group remains to be located, the choice being restricted to C(6) or C(10) to account for a *ddd* for *CH*OAc. That the proper choice is C(6) is suggested both by a small $^1H,^1H$ coupling of Me(18) and H_b–C(5) and by the fact that on irradiation at Me(18), there is a differential NOE enhancement at both H_b–C(5) and H–C(6). Finally, a $J = 10.3$ Hz for the coupling between H–C(6) and H_a–C(5) suggests a *trans* diaxial relationship for them and, therefore, the pseudoequatorial position for the AcO group as shown in structure (+)-**8**.

Examples of cembranoids which have all structural features of (+)-**8**, except for hydroxylation at different positions, have already been reported from tropical alcyonaceans such as 13-hydroxycembrene C from *Nephthea brassica* [4a] and *Nephthea* sp. [4b] and 14-hydroxycembrene C from *Lobophytum pauciflorum* [5a], *Sarcophyton glaucum* [5b], and *Sarcophyton* sp. [4a].

2.3. *On the Biogenesis.* Stimulated by the idea that preverecynarmin ((+)-**8**) could be a precursor of the briaranes (see [7]), we searched for the presence of further cembranoids in *A. maculata,* being thus gratified by the isolation of cembrene C (**9**) (from which (–)-**8** may derive *via* allylic oxidation) in trace amounts[5]). Although **9** has widespread occurrence in tropical alcyonaceans[6]), neither it nor any other cembranoid has ever been detected before this work in pennatulaceans or gorgonians. On the other hand, these two groups of cnidarians are the only known source of briarane diterpenoids. A hypothetic biogenesis of the briaranes from (+)-**8** is outlined in the *Scheme,* involving nucleophilic attack at C(8) by C(3) (see **10** → **11**).

Scheme



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[4]) H–C(2) and H–C(3) resonate at much the same field in C_6D_6; addition of $[(D_{27})Eu(fod)_3]$ gives rise to an *AB* system ($J_{AB} \approx 11$) with H–C(3) at lower field and broader (coupling with Me(18)) than H–C(2).

5) The search for **9** in *V. cynomorium* proved not to be practically feasible as this coral contains terpenoids in overall much lower concentration than *A. maculata.*

[6]) Cases in point are *Alcyonium flaccidum* [6a], *Alcyonium utinomii* [6b], *Lobophytum* sp. [6c], *Nephthea brassica* [4a], *Nephthea chabrolii* [6d], and *Nephthea* sp. [6e].

Experimental Part

1. *General.* All evaporations were carried out at reduced pressure. Column chromatography and flash chromatography (FC): *Merck* silica gel *60* (70–230 μm). Reverse-phase FC: *Merck RP-18 LiChroprep* (40–65 μm). HPLC: *Merck-LiChrosorb Si-60* (7 μm). Reverse-phase HPLC: *Merck-LiChrosorb RP-18* (7 μm). HPLC-CN: *Merck LiChrosorb CN* (7 μm). All HPLC columns were 25 × 1 cm with solvent flow 5 ml/min; monitoring by UV at 250 nm. Polarimetric data: *JASCO-DP-181* polarimeter. UV (λ_{max} in nm, ε in mol^{-1} 1 cm^{-1}) and IR ($\tilde{\nu}_{max}$ in cm^{-1}): *Perkin-Elmer-Lambda-3* and *Pye-Unicam-SP3-200* spectrometers, resp. NMR: *Varian-XL-300* (^{13}C-NMR at 75.43 MHz, ^{1}H-NMR at 300 MHz); probe temp. 22° if not otherwise stated; δ's (ppm) rel. to internal Me_4Si (= 0 ppm) and J in Hz; J from double irradiations, those > 0.5 Hz were confirmed by ^{1}H,^{1}H COSY [8] experiments (only the most significant correlations are reported, as δ (proton) → δ's (correlated protons)); 'small' indicates $J < 0.5$ Hz (confirmed by delayed COSY [8] experiments); multiplicities in ^{13}C-NMR from DEPT experiments [9]; ^{13}C,^{1}H-NMR shift-correlation experiments [10] and differential NOE's as in [1]. EI-MS (*m/z* (%)): home-built spectrometer based on the *ELFS-4-162-8-Extranuclear* quadrupole [11].

2. *Isolations.* Three fractions left from previous FC of *Armina maculata* extracts [1a], obtained with petroleum ether/Et_2O (first 85:15 (*a*) and then 3:1 (*b*)) and finally neat Et_2O (*c*), have now been examined. Evaporation of the eluate *a* gave 0.64 g of a residue which were subjected to FC with hexane/$(i\text{-}Pr)_2O$ 99.5:0.5; evaporation of this eluate gave 0.02 g of a residue which was subjected to reverse-phase HPLC with MeOH/H_2O 95:5: **9** (1.1 mg, t_R 14 min). Evaporation of eluate *b* gave 0.12 g of a residue which was subjected to reverse-phase HPLC with MeOH/H_2O 4:1: (−)-**6** (3.8 mg, t_R 14 min). Evaporation of eluate *c* gave 1.4 g of a residue which was subjected to reverse-phase FC with MeOH/H_2O 4:1 to give 0.25 g of a residue from which 8.5 mg of (−)-**5** and 2.8 mg of (−)-**7** were obtained by reverse-phase HPLC with MeOH/H_2O 7:3 (t_R 8 min) and 3:2 (t_R 15 min), resp. Another portion (6.8 g) of the previous dark oily residue from petroleum ether extractions of *Armina maculata* [1a] was subjected to FC with petroleum ether/Et_2O 85:15; evaporation of the eluate gave 0.49 g of a residue which was subjected to HPLC-CN with hexane. Evaporation of the eluate at t_R 6 min gave 6 mg of a residue which was subjected to HPLC with hexane/AcOEt 99.2:0.8: (+)-**8** (3.5 mg, t_R 10 min). This compound (1 mg) could also be isolated by the same procedure from *V. cynomorium*.

3. *Verecynarmin E* (= *(−)-(1R*,10R*,11S*,5Z)-11-Hydroxybriara-5,7,12,17-tetraen-14-one* = *(−)-(8aR*,12S*,12aR*,4Z)-7,8,8a,12,12a,13-Hexahydro-12-hydroxy-1,5,8a,12-tetramethylbenzo[4,5]cyclodeca[1,2-b]furan-9(6H)-one;* (−)-**5**). Colorless foam. $[\alpha]^{20}$ (λ [nm]) = −184.1 (589), −190.4 (577), −227.9 (546), −447.4 (435), −870.5 (365; c = 0.62, EtOH). UV (EtOH): 218 (13200), 264 (10100). ^{1}H-NMR (C_6D_6, 54.7°): 1.38, 2.59 (*dd*, J = 14.5, 10.5 and br. *dd*, resp., 2 H–C(2)); 1.84, 1.11 (2*m*, 2 H–C(3)); 2.32, 2.02 (br. *ddd* and *m*, resp., 2 H–C(4)); 6.05 (br. *q*, J(6,16) = 0.9, H–C(6)); 2.71 (br. *d*, J_{gem} = 16.5, J(9a,10) and J(9a,6) small, H_a–C(9)); 3.09 (*dd*, J_{gem} = 16.5, J(9b,10) = 9.9, H_b–C(9)); 2.99 (br. *d*, J(10,9a) small, J(10,9b) = 9.9, H–C(10)); 5.97 (*d*, J(12,13) = 10.0, H–C(12)); 5.80 (*d*, J(13,12) = 10.0, H–C(13)); 1.10 (*s*, 3 H–C(15)); 1.53 (br. *d*, J(16,6) = 0.9, 3 H–C(16)); 7.01 (*q*, J(18,19) = 1.1, H–C(18)); 1.92 (*d*, J(19,18) = 1.1, 3 H–C(19)); 0.87 (*s*, 3 H–C(20)). ^{1}H,^{1}H COSY (54.7°): 2.59 (H–C(2)) → 1.38 (H–C(2)), 1.82 (H–C(3)); 2.32 (H–C(4)) → 2.02 (H–C(4)), 1.82 (H–C(3)), 1.11 (H–C(3)); 2.02 (H–C(4)) → 2.32 (H–C(4)), 1.82 (H–C(3)), 1.11 (H–C(3)); 1.82 (H–C(3)) → 2.59 (H–C(2)), 2.32 (H–C(4)), 2.02 (H–C(4)), 1.11 (H–C(3)); 1.38 (H–C(2)) → 2.59 (H–C(2)), 1.11 (H–C(3)); 1.11 (H–C(3)) → 2.32 (H–C(4)), 2.02 (H–C(4)), 1.82 (H–C(3)), 1.38 (H–C(2)). MS: 314 (100, M^+), 299 (2, $[M - CH_3]^+$), 296 (3, $[M - H_2O]^+$), 281 (12, $[M - CH_3 - H_2O]^+$), 253 (4), 161 (20), 149 (5), 147 (12), 145 (15).

4. *Verecynarmin F* (= *(−)-(1R*,10S*,11R*,5Z)-Briara-5,7,12,17-tetraen-14-one* = *(−)-(8aR*,12R*,12aS*,4Z)-7,8,8a,12,12a,13-Hexahydro-1,5,8a,12-tetramethylbenzo[4,5]cyclodeca[1,2-b]furan-9(6H)-one;* (−)-**6**). $[\alpha]^{20}$ (λ [nm]) = −197.5 (589), −206.4 (577), −236.3 (546), −431.3 (435), −575.3 (365; c = 0.27, EtOH). UV (EtOH): 218 (12900), 253 (5700). ^{1}H-NMR (C_6D_6): 1.28 and 2.75 (2 br. *m*, 2 H–C(2)); 1.84, 1.16 (2 br. *m*, 2 H–C(3)); 2.23, 1.90 (2 br. *m*, 2 H–C(4)); 6.11 (br. *q*, J(6,16) = 1.5, J(6,9a) small, H–C(6)); 2.81 (br. *d*, J_{gem} = 16.8, J(9a,10) and J(9a,6) small, H_a–C(9)); 2.02 (*dd*, J_{gem} = 16.8, J(9b,10) = 9.3, H_b–C(9)); 1.52 (*m*, J(10,9b) = 9.3, J(10,11) = 10.0, J(10,9a) small, H–C(10)); 1.92 (*m*, irradiation at 0.66 → br. *d*, J(11,10) ≈ 10, H–C(11)); 5.92 (*dd*, J(12,13) = 10.3, J(12,11) = 1.5, H–C(12)); 5.94 (*d*, J(13,12) = 10.3, H–C(13)); 0.81 (br. *s*, 3 H–C(15)); 1.49 (br. *d*, J(16,6) = 1.5, 3 H–C(16)); 6.99 (*q*, J(18,19) = 1.2, H–C(18)); 1.76 (*d*, J(19,18) = 1.2, 3 H–C(19)); 0.66 (*d*, J(20,11) = 7.1, 3 H–C(20)). ^{1}H,^{1}H COSY: 2.75 (H–C(2)) → 1.84 (H–C(3)), 1.28 (H–C(2)); 2.23 (H–C(4)) → 1.90 (H–C(4)); 1.84 (H–C(3)), 1.16 (H–C(3)); 1.90 (H–C(4)) → 2.23 (H–C(4)), 1.84 (H–C(3)); 1.84 (H–C(3)) → 2.75 (H–C(2)), 2.23 (H–C(4)), 1.90 (H–C(4)), 1.16 (H–C(3)); 1.28 (H–C(2)) → 2.75 (H–C(2)), 1.16 (H–C(3)); 1.16 (H–C(3)) → 2.23 (H–C(4)), 1.84 (H–C(3)), 1.28 (H–C(2)). MS: 298 (100, M^+), 283 (4,

$[M - CH_3]^+$), 255 (2, $[283 - CO]^+$), 176 (6), 174 (10), 161 (26), 159 (29), 149 (30), 147 (20), 145 (35), 123 (13), 121 (10).

5. *Verecynarmin G* (= *(−)-(1*R*,4*S*,10*R*,11*R*,12*S*,14*S*,5Z)-11,12-Epoxy-4-hydroxybriara-5,7,17-trien-14-yl Acetate* = *(−)-(6*R*,8a*S*,9*R*,11*R*,12*S*,12a*S*,5Z)-11,12-Epoxy-6,7,8,8a,9,10,11,12,12a,13-decahydro-6-hydroxy-1,5,8a,12-tetramethylbenzo[4,5]cyclodeca[1,2-b]furan-9-yl Acetate*; (−)-**7**). $[\alpha]^{20}$ (λ [nm]) = −46.7 (589), −52.3 (577), −63.4 (546), −165.4 (435), −433.3 (365; *c* = 0.23, EtOH). UV (EtOH): 267 (13200). ^{1}H-NMR (C_6D_6, 55°): 1.30, 1.55 (2 br. *m*, 2 H−C(2)); 1.7–1.9 (br. *m*, 2 H−C(3)); 4.55 (br. *t*, $J(4,3) \approx 7$, H−C(4)); 6.24 (br. *q*, $J(6,16) = 1.5$, $J(6,9a)$ small, H−C(6)); 2.59 (br. *d*, $J_{gem} = 16.5$, $J(9a,10)$ and $J(9a,6)$ small, H_a−C(9)); 2.68 (*dd*, $J_{gem} = 16.5$, $J(9b,10) = 9.0$, H_b−C(9)); 2.35 (br. *d*, $J(10,9b) = 9.0$, $J(10,9a)$ small, H−C(10)); 2.60 (br. *d*, $J(12,13\alpha) = 5.8$, $J(12,13\beta)$ and $J(12,14)$ small, H−C(12)); 1.85 (*ddd*, $J_{gem} = 16.5$, $J(13\alpha,12) = 5.8$, $J(13\alpha,14) = 2.6$, H_α−C(13)); 1.99 (br. *dd*, $J_{gem} = 16.5$, $J(13\beta,14) = 3.3$, $J(13\beta,12)$ small, H_β−C(13)); 4.52 (br. *s*, superimposed by H−C(4), $J(14,13\beta) = 3.3$, $J(14,13\alpha) = 2.6$, $J(14,12)$ small, H−C(14)); 0.80 (br. *s*, $J(15,2)$ small, 3 H−C(15)); 1.78 (br. *d*, $J(16,6) = 1.5$, 3 H−C(16)); 6.99 (*q*, $J(18,19) = 1.5$, H−C(18)); 1.89 (*d*, $J(19,18) = 1.5$, 3 H−C(19)); 0.98 (*s*, 3 H−C(20)); 1.69 (*s*, Ac); 0.68 (br. *s*, OH). ^{1}H,^{1}H COSY: 1.30 (H−C(2)) → 1.55 (H−C(2)), 1.7 (H−C(3)); 1.55 (H−C(2)) → 1.30 (H−C(2)), 1.7 (H−C(3)), 1.9 (H−C(3)), 0.80[7]) (3 H−C(15)); 1.7 (H−C(3)) → 1.30 (H−C(2)), 1.55 (H−C(2)), 1.9 (H−C(3)), 4.55 (H−C(4)); 1.9 (H−C(3)) → 1.55 (H−C(2)), 1.7 (H−C(3)), 4.55 (H−C(4)); 4.55 (H−C(4)) → 1.7 (H−C(3)), 1.9 (H−C(3)), 1.78[7]) (3 H−C(16)). MS: 374 (100, M^+), 359 (2, $[M - CH_3]^+$), 356 (6, $[M - H_2O]^+$), 296 (1, $[356 - AcOH]^+$), 281 (6, $[296 - CH_3]^+$), 177 (69), 173 (12), 161 (21), 159 (48), 145 (28), 135 (93).

6. *Cembrene C* (= *(all-*E*)-Cembra-1,3,7,11-tetraene* = *(all-*E*)-1,7,11-Trimethyl-4-(1-methylethyl)cyclotetradeca-1,3,7,11-tetraene*; **9**). ^{1}H-NMR (C_6D_6): 6.24 (*X* of A_3XY, $J(XY) = 11.2$, $J(XA) = 0$, H−C(2)); 6.16 (*Y* of A_3XY, $J(YX) = 11.2$, $J(YA) = 1.2$, H−C(3)); 5.17 (br. *t*, $J = 7.0$, H−C(7)); 5.10 (br. *t*, $J = 7.0$, H−C(11)); 2.37 (*m*, H_a−C(14)); 2.30 (*sept.*, $J = 6.8$, H−C(15)); 1.07 (*d*, $J = 6.8$, 3 H−C(16), 3 H−C(17)); 1.72 (A_3 of A_3XY, $J(AY) = 1.2$, $J(AX) = 0$, 3 H−C(18)); 1.59 (br. *s*, 3 H−C(19)); 1.48 (br. *s*, 3 H−C(20)); 2.13 (*m*, remaining 11 H). MS and UV: matching data of [6e].

7. *Preverecynarmin* (= *(+)-(all-*E*)-Cembra-1,3,7,11-tetraen-6-yl Acetate* = *(+)-(all-*E*)-3,7,13-Trimethyl-10-(1-methylethyl)cyclotetradeca-2,6,10,12-tetraenyl Acetate*; (+)-**8**). $[\alpha]^{20}$ (λ [nm]) = +116.2 (589), +145.3 (546), +277.9 (435), +528.0 (365; *c* = 0.16, EtOH). UV (EtOH): 251 (15800), 243 (sh), 260 (sh). ^{1}H-NMR (C_6D_6): 6.15 (br. *s*, H−C(2), H−C(3)); 2.42 (br. *dd*, $J_{gem} = 12.5$, $J(5a,6) = 10.3$, $J(5a,3)$ small, H_a−C(5)); 2.50 (br. *dd*, $J_{gem} = 12.5$, $J(5b,6) = 3.5$, $J(5b,18)$ and $J(5b,3)$ small, H_b−C(5)); 5.92 (*ddd*, $J(6,5a) = 10.3$, $J(6,5b) = 3.5$, $J(6,7) = 9.3$, H−C(6)); 5.22 (br. *d*, $J(7,6) = 9.3$, $J(7,19) = 1.4$, H−C(7)); 5.05 (*m*, H−C(11)); 2.65 (*m*, H_a−C(14)); 2.25 (br. *sept.*, $J(15,16) = J(15,17) = 6.9$, $J(15,2)$ small, H−C(15)); 1.02 (*d*, $J(16,15) = 6.9$, 3 H−C(16)); 1.03 (*d*, $J(17,15) = 6.9$, 3 H−C(17)); 1.79 (br. *s*, $J(18,3)$ and $J(18,5b)$ small, 3 H−C(18)); 1.57 (br. *d*, $J(19,7) = 1.4$, 3 H−C(19)); 1.52 (br. *d*, $J(20,11) = 1.2$, 3 H−C(20)); 1.72 (*s*, Ac); 2.05 (*m*, 2 H−C(9), 2 H−C(10), 2 H−C(13), H_b−C(14)). ^{1}H,^{1}H COSY: 6.15 (H−C(3)) → 1.79 (3 H−C(18)), 2.42[7]) (H_a−C(5)), 2.50[7]) (H_b−C(5)); 5.92 (H−C(6)) → 5.22 (H−C(7)), 2.50 (H_b−C(5)), 2.42 (H_a−C(5)); 5.22 (H−C(7)) → 5.92 (H−C(6)), 1.57 (3 H−C(19)), 2.05[7]) (2 H−C(9)); 2.50 (H_b−C(5)) → 5.92 (H−C(6)), 2.42 (H_a−C(2)), 1.79[7]) (3 H−C(18)), 6.15[7]) (H−C(3)); 2.42 (H_a−C(5)) → 5.92 (H−C(6)), 2.50 (H_b−C(5)), 6.15[7]) (H−C(3)); 1.79 (3 H−C(18)) → 6.15 (H−C(3)), 2.50[7]) (H_b−C(5)). Differential NOE (C_6D_6, irradiated proton(s) → positive NOE effect (%) on the observed proton(s)): H−C(2) → 5 (H−C(15)), 2 (3 H−C(16) and 3 H−C(17)), 5 (3 H−C(18)); H−C(3) → 12 (H_a−C(14)), 4 (H−C(11)), 3 (H−C(7)), 8 (H_a−C(5)); 3 H−C(18) → 10 (H−C(2)), 6 (H_b−C(5)), 5 (H−C(6)); 3 H−C(19) → 10 (H−C(6)), 2 (superimposed H's at 2.05); 3 H−C(20) → 2 (superimposed H's at 2.05). MS: 330 (2, M^+), 270 (84, $[M - AcOH]^+$), 255 (4, $[270 - CH_3]^+$), 227 (13, $[270 - C_3H_7]^+$), 202 (13), 187 (25), 159 (86), 121 (100).

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[7]) Data derived from delayed COSY experiments.

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