New Cembranoid Diterpenes and a Geranylgeraniol Derivative from the Common Caribbean Sea Whip *Eunicea succinea*[1,2]

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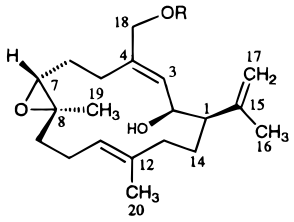
A recent collection and extraction of the common Caribbean sea whip *Eunicea succinea* from Puerto Rico has produced four previously undescribed representatives of the cembrane family of diterpenes (**2**, **3**, **4**, and **6**). A new geranylgeraniol derivative, **8**, was also isolated as a minor constituent. The chemical structures of the new compounds were carefully established by spectroscopic and chemical methods in addition to detailed NMR spectral comparisons with known cembranoid models from *Eunicea*.

Sea whips of the genus *Eunicea* are diverse and abundant in the Caribbean region.[4] Unfortunately, difficulties in collecting taxonomically homogeneous samples have hampered their chemical study, and many *Eunicea* species remain to be investigated comprehensively.[5] For several years, our laboratory has been interested in the study of the gorgonian species *Eunicea succinea* and *Eunicea mammosa* partly because of their ability to biosynthesize large amounts of bioactive cembranolide-type diterpenes.[6,7] Our last investigation of the cytotoxic constituents of *E. succinea* (Pallas) (phylum Coelenterata, class Anthozoa, subclass Octocorallia, order Gorgonacea, family Plexauridae) from Puerto Rico resulted in the discovery of seven new cembranolide diterpenes.[8] All of the compounds isolated constituted additional examples of Caribbean cembranolides displaying remarkable arrays of functional groups across the entire cembrane skeleton. As part of our ongoing search for new bioactive cembranolides from the Caribbean Sea, we now describe the isolation and structure elucidation of five previously unreported diterpenoids from the same specimen of *E. succinea* collected near Mona Island off the west coast of Puerto Rico.



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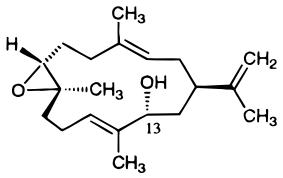

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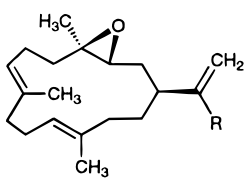

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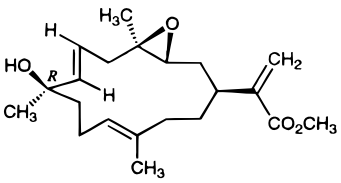
5 R= CH_2OH



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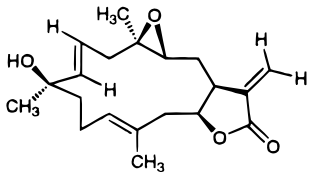

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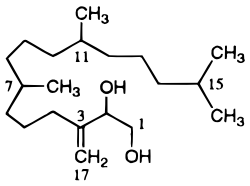

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Results and Discussion

Specimens of *E. succinea* were frozen and freeze-dried prior to extraction with a mixture of 1:1 MeOH−$CHCl_3$. The main fractions obtained from the hexane extract consisted of several well-known α-methylene-γ-cembranolides such as euniolide,[9] eupalmerin acetate,[10] eunicin,[11] and 12,13-bisepieupalmerin.[12] Also from the hexane extract, lesser amounts of the recently discovered cembranolide diterpenes 12,13-bisepieupalmerin epoxide, 12,13-bisepiuprolide-B, 12,13-bisepiuprolide-B acetate, uproeunicin, 12,13-bisepiuprolide-D acetate, eunicenolide, and uproeuniolide (**7**) were isolated.[8] In addition, four new cembranoid diterpenes described here (**2**−**4** and **6**) and a rare geranylgeraniol derivative, **8**, were isolated and purified after further conventional chromatographic procedures of the same hexane extract (see the Experimental Section).

A molecular formula of $C_{22}H_{34}O_4$ was established for compound **2** from HREIMS plus ^1H and ^{13}C NMR data. The IR spectrum contained a carbonyl band at 1740 cm^{-1} consistent with the presence of an ester group in addition to strong hydroxyl and epoxide stretching bands at 3467 and 1229 cm^{-1}, respectively. The ^{13}C NMR spectrum exhibited 22 signals ($4CH_3$, $8CH_2$, 5CH, and 5C) whose chemical shift values and multiplicities hinted at the presence of an epoxide [64.6 (d, C-7) and δ 60.2 (s, C-8)], two trisubstituted olefins [δ 132.1 (d, C-3) and 135.4 (s, C-4); δ 124.8 (d, C-11) and 134.5 (s, C-12)], a terminal olefin [δ 113.9 (t, C-17) and 145.5 (s, C-15)], two oxygen-bearing carbons [δ 68.3 (d, C-2) and δ 67.0 (t, C-18)], and one ester carbonyl [δ 170.7 (s, C-21)]. Shortly after its purification, we realized that the ^{13}C NMR spectrum of compound **2** was remarkably reminiscent of that reported for asperdiol (**1**), a known cembranoid diterpene isolated by Weinheimer and coworkers from the related gorgonian species *E. asperula*.[13] A side-by-side comparison between the ^{13}C NMR data of compound **2** and those of asperdiol (see Table 2)

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Table 1. ^{1}H NMR (300 MHz) Spectral Data for Compounds **2**−**4** and **6**[a] (δ, int, mult, *J* (Hz))

H	2	3	4	6
1	2.04, 1H, m	2.01, 1H, m	2.79, 1H, m	2.70, 1H, m
2	4.48, 1H, m	2.16, 1H, m; 2.18, 1H, m	1.41, 1H, m; 1.79, 1H, m	1.47, 1H, m; 1.81, 1H, m
3	5.46, 1H, br d, 7.8	5.04, 1H, br t, 6.9	2.83, 1H, dd, 3.6, 9.3	2.79, 1H, dd, 3.9, 9.0
5	2.31, 1H, m	2.09, 1H, m	1.25, 1H, m	2.62, 1H, m
	2.31, 1H, m	2.15, 1H, m	2.03, 1H, m	2.64, 1H, m
6	1.48, 1H, m	1.29, 1H, m	2.06, 1H, m	5.63, 1H, m
	1.81, 1H, m	1.76, 1H, m	2.15, 1H, m	
7	2.68, 1H, dd, 4.8, 6.3	2.73, 1H, dd, 2.7, 9.9	5.10, 1H, br t, 5.7	5.43, 1H, d, 15.9
9	1.31, 1H, m	1.25, 1H, m	2.06, 1H, m	1.21, 1H, m
	2.01, 1H, m	2.06, 1H, m	2.14, 1H, m	1.99, 1H, m
10	2.18, 2H, m	2.24, 1H, m	2.15, 1H, m	2.00, 1H, m
		2.27, 1H, m	2.19, 1H, m	2.18, 1H, m
11	5.12, 1H, br t, 6.9	5.33, 1H, br t, 6.9	5.19, 1H, br t, 6.6	5.07, 1H, br m
13	2.00, 2H, m	3.87, 1H, dd, 3.9, 10.5	1.81, 1H, m	1.43, 1H, m
			2.09, 1H, m	1.52, 1H, m
14	1.50, 1H, m	1.76, 1H, m	1.65, 1H, m	1.58, 1H, m
	1.73, 1H, m	1.82, 1H, m	1.76, 1H, m	1.60, 1H, m
16	1.75, 3H, s	1.66, 3H, s	9.52, 1H, s	
17	4.76, 1H, br s	4.63, 1H, br s	6.02, 1H, s	5.50, 1H, br s
	4.96, 1H, br s	4.70, 1H, br s	6.25, 1H, s	6.24, 1H, br s
18	4.48, 1H, br s	1.62, 3H, s	1.19, 3H, s	1.24, 3H, s
	4.52, 1H, br s			
19	1.19, 3H, s	1.22, 3H, s	1.56, 3H, s	1.22, 3H, s
20	1.61, 3H, s	1.66, 3H, s	1.62, 3H, s	1.62, 3H, s
21				3.70, 3H, s
22	2.07, 3H, s			

[a] ^{1}H NMR spectra were recorded at 25 °C in $CDCl_3$. Chemical shifts are given in δ units downfield from Me_4Si. Assignments were aided by ^{1}H-^{1}H COSY, HETCOR, selective INAPT, HMBC and NOESY experiments.

Table 2. ^{13}C NMR (75 MHz) Spectral Data for Compounds **1**−**4** and **6**[a] (δ (mult))

C	1[b]	2	3	4	6
1	50.4 (d)	50.3 (d)	40.6 (d)	31.2 (d)	37.7 (d)
2	68.3 (d)	68.3 (d)	24.0 (t)	33.7 (t)	34.9 (t)
3	128.5 (d)	132.1 (d)	123.1 (d)	62.5 (d)	61.3 (d)
4	139.3 (s)	135.4 (s)	135.1 (s)	60.7 (s)	60.3 (s)
5	25.7 (t)	26.2 (t)	38.8 (t)	38.3 (t)	40.9 (t)
6	26.4 (t)	26.5 (t)	33.5 (t)	23.6 (t)	126.6 (d)
7	64.7 (d)	64.6 (d)	63.3 (d)	124.9 (d)	137.9 (d)
8	60.2 (s)	60.2 (s)	60.7 (s)	135.1 (s)	73.0 (s)
9	37.3 (t)	37.4 (t)	38.0 (t)	39.4 (t)	37.8 (t)
10	23.9 (t)	24.0 (t)	24.1 (t)	24.5 (t)	23.0 (t)
11	124.5 (d)	124.8 (d)	127.2 (d)	123.9 (d)	122.5 (d)
12	135.4 (s)	134.5 (s)	135.8 (s)	133.1 (s)	135.3 (s)
13	35.9 (t)	36.0 (t)	75.2 (d)	35.2 (t)	39.8 (t)
14	27.9 (t)	28.0 (t)	37.2 (t)	30.3 (t)	27.4 (t)
15	145.7 (s)	145.5 (s)	147.6 (s)	154.5 (s)	142.8 (s)
16	22.2 (q)	22.5 (q)	18.4 (q)	194.2 (d)	167.4 (s)
17	113.5 (t)	113.9 (t)	111.0 (t)	133.5 (t)	124.4 (t)
18	65.4 (t)	67.0 (t)	16.2 (q)	16.9 (q)	16.4 (q)
19	16.5 (q)	16.6 (q)	16.7 (q)	16.9 (q)	27.2 (q)
20	15.7 (q)	15.8 (q)	13.0 (q)	15.7 (q)	17.7 (q)
21		170.7 (s)			51.8 (q)
22		20.9 (q)			

[a] ^{13}C NMR spectra were recorded in $CDCl_3$ at 25 °C. Number of attached protons were determined by APT experiments. Assignments were aided by ^{1}H−^{1}H COSY, selective INAPT, HETCOR, and HMBC experiments. [b] Chemical shift values were taken directly from ref 13b (some of the original atom assignments have been corrected).

rapidly pinpointed their structural similarities. Nevertheless, some minor differences between these compounds were observed in the ^{13}C NMR spectra: the signals ascribed to C-3, C-4, and Me-18 in **2** showed considerable differences in chemical shifts and had shifted from δ 128.5 (d), 139.3 (s), and 65.4 (t) in asperdiol (**1**) to δ 132.1 (d), 135.4 (s), and 67.0 (t) in **2**, respectively. Moreover, compound **2** displayed two extra resonances at δ 170.7 (s) and 20.9 (q) that were not present in asperdiol. Acetylation of the primary hydroxyl group at C18 in asperdiol would account for these spectral differences. Consideration of ^{1}H and ^{13}C NMR data as well as other spectral data allowed the complete structure of this metabolite to be assigned as asperdiol acetate (**2**). The C-7(*S*), C-8(*S*) stereochemistry of the epoxide in **2** was argued on the basis of the ^{13}C NMR chemical shift values for C-7 and C-19.[13,14] Also, multiple NOE's detected during a PSNOESY experiment clearly correlated with a Dreiding model representing the relative stereochemistry shown in structure **2**.

7(*S*),8(*S*)-Epoxy-13(*R*)-hydroxy-1(*R*)-cembrene-A (**3**) was isolated as a colorless oil with a molecular formula of $C_{20}H_{32}O_2$ established from HREIMS and ^{13}C NMR data. Strong IR bands due to hydroxyl (3437 cm^{-1}) and epoxide (1242 cm^{-1}) functionalities were clearly detected. The ^{1}H NMR spectrum showed only two signals at δ 2.73 and 3.87 that could be attributed to methine protons on carbon atoms bearing oxygen (H-7 and H-13, respectively). The ^{13}C NMR spectrum exhibited 20 signals (4CH_3, 7CH_2, 5CH, and 4C) whose chemical shift values and multiplicities indicated the presence, as in asperdiol acetate (**2**), of an epoxide [δ 60.7 (s, C-8) and δ 63.3 (d, C-7)] and three olefins: two were trisubstituted [δ 123.1 (d, C-3) and 135.1 (s, C-4); δ 127.2 (d, C-11) and 135.8 (s, C-12)] and one was terminal [δ 111.0 (t, C-17) and 147.6 (s, C-15)]. On the other hand, unlike **2**, no ester carbonyl carbon and only one additional oxygen-bearing carbon [δ 75.2 (d, C-13)] were detected. A comparison between the NMR spectral data of compound **3**, including the results of ^{1}H−^{1}H COSY and HMBC experiments, and those of asperdiol acetate (**2**) suggested a subtle structural relationship between these compounds. For instance, from these data it became evident that each compound appeared to have a C-7(*S*),8-(*S*) epoxide functionality, an isopropenyl group attached to C-1, two trisubstituted olefins across C-3,4 and C-11,12, and an allylic secondary hydroxyl group. Nevertheless, several major differences between these compounds were deduced from their 1D and 2D NMR spectral data: the signals and correlations ascribed to

the secondary carbinol functionality in **3** placed the alcohol at C-13 (the secondary alcohol proton in the ^{1}H NMR spectrum appeared as a doublet of doublets at δ 3.87 consistent with it being allylic and adjacent to a methylene group) and both trisubstituted olefins bore a methyl group and had *E* stereochemistry. Specifically, the ^{13}C NMR shifts in **3** at δ 63.3 (d, C-7) and 16.7 (q, C-19) distinctively established the C-7(*S*),8(*S*) configuration around the epoxide[13,14] and those at δ 16.2 (Me-18) and δ 13.0 (Me-20) indicated the *E* configuration about the trisubstituted olefins.[15] To address the question of stereochemistry at C-13, we performed MM+ molecular mechanics calculations on the diastereomer with the isopropenyl/H-13 groups cis [that is, C-1(*R*), C-13(*R*)] and the diastereomer with those groups trans [C-1(*R*), C-13(*S*)]. Both isomers had similar steric energies after geometry optimization, and there were no obvious predicted differences in NOE to distinguish them. This was consistent with the small $\Delta\delta$ observed between H-14α and H-14β in the ^{1}H NMR data (Table 1). The torsional angles between the two protons on C-14 and the single proton on C-13 were, however, distinct in the two isomers. For the trans isomer, the MM+ calculations predicted H-14,C-14,C-13,H-13 angles of 56° and 59°, corresponding (through the Karplus relationship) to couplings of 4 and 3 Hz, respectively. For the cis isomer, the angles were 52° and 155°, corresponding to coupling constants of 4 and 11 Hz. The ^{1}H$-^1$H COSY NMR spectrum revealed that H-13 was coupled to two protons. According to our analysis above, one was H-14 (J = 3.9 Hz) and the other was H-14′ (J = 10.5 Hz). This large coupling to H-13 was consistent with the torsional angles calculated for the cis isomer. These results agreed with published data for analogous compounds (e.g., 13-hydroxycembrenes);[16] therefore, we tentatively assigned the relative configuration of the hydroxyl group as 13(*R*).

The HREIMS and ^{13}C NMR data for compound **4** were consistent with a molecular formula of $C_{20}H_{30}O_2$. An intense IR band at 1715 cm^{-1} was ascribed to a carbonyl group. As in the previous metabolites, the ^{13}C NMR spectrum exhibited signals due to an epoxide and three olefins: one was terminal and two were methyl-bearing trisubstitued olefins. The ^{1}H NMR spectrum in $CDCl_3$ showed three sharp singlets at δ 9.52 (1H, H-16), 6.25 (1H, H-17), and 6.02 (1H, H-17′), suggesting the presence in **4** of an α,β-unsaturated aldehyde moiety. This observation was supported by a strong UV absorption in MeOH at λ_{max} = 208 nm (ϵ 7000). A combination of ^{1}H$-^1$H COSY, HETCOR, and selective INAPT experiments established the relative position of all the functional groups within the cembrane skeleton. Consideration of the NMR data as well as other spectral data allowed the complete structure of this metabolite to be assigned as pseudoplexaural (**4**). To confirm this contention, we treated pseudoplexaurol (**5**),[17] a known compound previously isolated in this laboratory from the gorgonian *Pseudoplexaura porosa*, with active 85% MnO_2 in CH_2Cl_2 at 25 °C to give a colorless oil that was identical in every respect to natural product **4**.

The major compound **6**, named uproeunioloic acid methyl ester, was an optically active oil of formula $C_{21}H_{32}O_4$ as determined by HREIMS and ^{13}C NMR data. The IR spectrum showed absorptions ascribable to hydroxyl, epoxide, and ester functionalities. The ^{1}H NMR spectrum showed signals for a 1,2-disubstituted double bond [δ 5.63, (1H, m, H-6) and δ 5.43 (1H, d, J = 15.9 Hz, H-7)], a methyl-bearing trisubstituted double bond [δ 1.62 (3H, s, Me-20); δ 5.07 (1H, br m, H-11)], two methyl groups on quaternary carbons bearing oxygen [δ 1.22 (3H, s, Me-19); δ 1.24 (3H, s, Me-18)], an allylic methine at δ 2.70 (m, H-1), an epoxymethine proton at δ 2.79 (dd, J = 3.9, 9.0 Hz, H-3), and a carbomethoxy group at δ 3.70 (3H, s, Me-21). The ^{13}C NMR and APT spectra showed resonance lines with adequate multiplicities to support these assignments. As before, ^{1}H$-^1$H COSY, HETCOR, and HMBC experiments clearly established the relative positions of all the functional groups within the cembrane carbon framework. These data showed that compound **6** was structurally related to the known cembranolide uproeuniolide (**7**), a metabolite recently isolated by us from this specimen of *E. succinea*.[8] However, unlike uproeuniolide, compound **6** did not have a cis-fused α-methylene-γ-butyrolactone moiety attached to C-1 and C-14 of the cembrane skeleton. The large coupling constant (15.9 Hz) observed in **6** for the Δ^6 ethylenic protons and the strong upfield shift experienced by C-8 (δ 73.0) clearly suggested the trans configuration.[7] The relative stereochemistry about the tertiary carbinol was assigned with confidence as C-8(*R*), inasmuch as the PSNOESY experiment revealed that protons H-5/H-7 and H-7/Me-19 were clearly within NOE proximity. Moreover, the C-8(*R*) configuration depicted in **6** was also consistent with the ^{13}C NMR chemical shift value (in $CDCl_3$ solution) observed for Me-19 (δ 27.2).[7] The remaining NOE's observed for **6** clearly correlated with a Dreiding model depicting the relative stereochemistry shown. In general, these results suggested a possible biogenetic relationship between compound **6** and uproeuniolide (**7**).

Compound **8** had a molecular formula of $C_{20}H_{40}O_2$ as deduced from HREIMS and ^{13}C NMR data. The IR spectrum contained a very intense absorption for hydroxyl (3410 cm^{-1}) functionalities and the ^{1}H NMR spectrum revealed prominent signals for three protons attached to carbons bearing oxygen [δ 4.20 (1H, dd, J = 3.0, 7.5 Hz, H-2), δ 3.70 (1H, dd, J = 3.3, 11.4 Hz, H-1) and δ 3.53 (1H, dd, J = 7.5, 11.4 Hz, H-1′)]. In addition to these signals, the proton spectrum contained two olefinic singlets at δ 5.12 (1H, H-17) and δ 4.97 (1H, H-17′) and a series of overlapped signals near δ 1.60$-$0.90 (19H, complex multiplet) ascribable in part to four secondary methyl groups. In the ^{13}C NMR spectrum only two olefinic signals were detected at δ 148.7 (s, C-3) and δ 110.5 (t, C-17). From these data, the presence of a terminal methylene group in the molecule was deduced. Signals for two oxygenated carbon signals at δ 75.0 (d, C-2) and δ 65.6 (t, C-1) were also observed. When the molecular formula and the NMR data of **8** were compared with those of **2**$-$**6**, it was clear that the former metabolite was not cembranoid but was instead an acyclic diterpene related to geranylgeraniol. A ^{1}H$-^1$H COSY experiment revealed strong geminal coupling between the signals at δ 3.70 and 3.53 (H-1/H-1′) and vicinal coupling between the latter protons and the signal at δ 4.20 (H$-$2). H-2, in turn, correlated with both H-17's (δ 5.12 and 4.97) indicating the proximity of the olefin to the terminal 1,2-diol functionality. The remaining structural features were quickly deduced

from interpretation of the NMR data and from careful analysis of the fragment ions observed in the HREIMS. Thus, we proposed structure **8**, devoid of relative stereochemistry at C-2, C-7, and C-11, for this acyclic diterpenoid metabolite.[18]

In the present work, we report the structures of four new cembranoid diterpenes and one geranylgeraniol derivative from the common Caribbean sea whip *E. succinea*. The NCI in vitro primary disease-oriented antitumor screen was used to ascertain the cytotoxic properties of asperdiol acetate (**2**), which displayed a GI_{50} value of 6.25×10^{-7} against one CNS cancer cell line (SNB-75) and 8.28×10^{-6} against both a melanoma (M14) and a breast cancer (HS 578T) cell line. Asperdiol acetate also displayed moderate nonselective cytotoxicity against the rest of the NCI panel cell lines in the concentration range of 10^{-5} M.

Experimental Section

General Experimental Procedures. For general experimental procedures, see Rodríguez and Boulanger.[19] Calculations in MM+ were performed on SPARTAN 4.1 (Wavefunction, Inc., Irvine, CA 92715) and implemented on a Silicon Graphics IRIS-INDIGO XS24 4000 workstation.

Collection and Extraction Procedures. The Caribbean gorgonian *E. succinea* was collected by scuba in November 1992 from Mona Island, Puerto Rico. The gorgonian was freeze-dried upon arrival and kept frozen until extraction. A voucher specimen (no. MIES-001) is stored at the Chemistry Department of the University of Puerto Rico, Río Piedras campus. The dried organism (2.5 kg) was blended with MeOH:$CHCl_3$ (1:1), and after filtration the crude extract was evaporated under vacuum to yield a residue (322.9 g) that was partitioned between hexane and H_2O. The hexane extract was concentrated to yield 170.9 g of a dark green oily residue that was later dissolved in toluene and filtered. The resulting filtrate was concentrated (168.9 g), loaded onto a large size exclusion column (Bio-Beads SX-2), and eluted with toluene. The combined terpenoid-rich fractions (TLC guided) were concentrated to a dark yellow oil (118.6 g) and chromatographed over a large silica gel column (3 kg) using 30% EtOAc in hexane. From this column 14 fractions were obtained, the less polar of which consisted of complex mixtures of unidentified sterols and fatty acid derivatives (3.8 g) and the following known cembranoid diterpenes: pseudoplexauric acid methyl ester[20] (29 g), euniolide[9] (24 g), succinolide[21] (150 mg), and eupalmerin acetate[10] (12.9 g). The more polar portion of the extract was divided roughly into fractions H-6 to H-14 on the basis of TLC analyses. From several of these fractions five known cembranolides were identified: 12,13-bisepieupalmerin acetate[20] (845 mg), 14-deoxycrassin[17] (225 mg), eunicin[11] (537 mg), 12,13-bisepieupalmerin[12] (3.0 g), and uprolide-B acetate[7] (8.3 mg). Work involving fractions 8, 12, and 13 led to cembranolide diterpenes 12,13-bisepieupalmerin epoxide, 12,13-bisepiuprolide-B, 12,13-bisepiuprolide-B acetate, uproeunicin, 12,13-bisepiuprolide-D acetate, eunicenolide, and uproeuniolide (**7**).[8] Fraction H-6 (2.3 g) was chromatographed over silica gel (90 g) with 10% EtOAc in hexane, affording subfractions A−Q, one of which was pseudoplexaural (**4**) (2.8 mg). Two subfractions (H-6N, O) were combined and subjected to column chromatography over silica gel (8 g) using 3% EtOAc in $CHCl_3$ to afford 7(*S*),8(*S*)-epoxy-13(*R*)-hydroxy-1(*R*)-cembrene-A (**3**) (17.7 mg). Column chromatography on silica gel (250 g) of fraction H-8 (5.22 g) with 45% EtOAc in hexane also afforded several subfractions. One of them (H-8C; 118.4 mg) was chromatographed over silica gel (7 g) with 5% acetone in $CHCl_3$ to yield geranylgeraniol derivative **8** (8.4 mg). Another subfraction (H-8F; 1.92 g) was chromatographed successively over two silica gel columns [the first using 5% 2-propanol in hexane (86 g) and the second 2% acetone in $CHCl_3$ (40 g)] and reversed-phase HPLC (Ultrasphere-ODS with 30% H_2O in MeOH) to give asperdiol acetate (**2**) (9.8 mg). A small amount of material (882 mg) generated during the purification of H-8F was also subjected successively to column chromatography [first on silica gel (80 g) with 2% acetone in $CHCl_3$ and then on silica gel (8 g) with 20% acetone in hexane] and reversed-phase HPLC (Zorbax-C8 with 40% H_2O in MeOH) leading to pure uproeunioloic acid methyl ester (**6**) (60 mg).

Asperdiol acetate (2): colorless oil; $[\alpha]^{25}_D$ −52.4° (*c* 2.5, $CHCl_3$); IR (neat) 3467, 3068, 2927, 2856, 1740, 1640, 1453, 1381, 1229, 1053, 1025, 963, 885, 800 cm^{-1}; UV λ_{max} (MeOH) 206 nm (ϵ 9900); ^1H NMR (300 MHz, $CDCl_3$) see Table 1; ^{13}C NMR (75 MHz, $CDCl_3$) see Table 2; EIMS *m/z* 362 (0.2), 344 (4), 302 (6), 284 (11), 152 (35), 135 (45), 121 (48), 109 (67), 95 (84), 81 (100), 69 (62); HREIMS *m/z* $[M]^+$ 362.2440 (calcd for $C_{22}H_{34}O_4$ 362.2457).

7(*S*),8(*S*)-Epoxy-13(*R*)-hydroxy-1(*R*)-cembrene-A (3): colorless oil; $[\alpha]^{25}_D$ −8.1° (*c* 4.2, $CHCl_3$); IR (neat) 3437, 2928, 2871, 2856, 1455, 1377, 1242, 1062, 901, 756, 666 cm^{-1}; UV λ_{max} (MeOH) 218 nm (ϵ 3400); ^1H NMR (300 MHz, $CDCl_3$) see Table 1; ^{13}C NMR (75 MHz, $CDCl_3$) see Table 2; EIMS *m/z* 304 (1), 286 (2), 159 (16), 145 (21), 133 (31), 119 (38), 107 (53), 93 (72), 81 (92), 67 (57), 55 (100); HREIMS *m/z* $[M]^+$ 304.2391 (calcd for $C_{20}H_{32}O_2$ 304.2402).

Pseudoplexaural (4): colorless oil; $[\alpha]^{25}_D$ −2.8° (*c* 1.4, $CHCl_3$); IR (neat) 2962, 2922, 2853, 1715, 1456, 1379, 1260, 1160, 1075, 1038, 802, 756, 667 cm^{-1}; UV λ_{max} (MeOH) 208 nm (ϵ 7000); ^1H NMR (300 MHz, $CDCl_3$) see Table 1; ^{13}C NMR (75 MHz, $CDCl_3$) see Table 2; EIMS *m/z* 302 (6), 284 (4), 269 (2), 159 (11), 145 (16), 133 (24), 119 (30), 107 (45), 93 (58), 81 (100), 79 (49), 67 (75), 55 (87); HREIMS *m/z* $[M]^+$ 302.2212 (calcd for $C_{20}H_{30}O_2$ 302.2246).

Uproeunioloic acid methyl ester (6): colorless oil; $[\alpha]^{25}_D$ −3.6° (*c* 12.9, $CHCl_3$); IR (neat): 3451, 2961, 2925, 2866, 1715, 1626, 1439, 1377, 1260, 1193, 1155, 1072, 951, 869, 818, 800, 755, 665 cm^{-1}; UV λ_{max} (MeOH) 222 nm (ϵ 4000); ^1H NMR (300 MHz, $CDCl_3$) see Table 1; ^{13}C NMR (75 MHz, $CDCl_3$) see Table 2; EIMS *m/z* 348 (8), 330 (7), 179 (22), 161 (33), 147 (38), 133 (51), 119 (62), 107 (73), 95 (86), 93 (100), 81 (90), 67 (60), 55 (92); HREIMS *m/z* $[M]^+$ 348.2302 (calcd for $C_{21}H_{32}O_4$ 348.2301).

Geranylgeraniol derivative 8:[18] colorless oil; $[\alpha]^{25}_D$ +1.0° (*c* 3.9, $CHCl_3$); IR (neat) 3410, 2953, 2926, 2869, 2857, 1462, 1377, 1260, 1239, 1169, 1068, 1033, 980, 903, 804, 736 cm^{-1}; UV λ_{max} (MeOH) 206 nm (ϵ 3100); ^1H NMR (300 MHz, $CDCl_3$) δ 5.12 (1H, br s, H-17), 4.97 (1H, br s, H-17′), 4.20 (1H, dd, J = 3.0, 7.5 Hz, H-2), 3.70 (1H, dd, J = 3.3, 11.4 Hz, H-1), 3.53 (1H, dd, J = 7.5, 11.4 Hz, H-1′), 2.20−1.86 (2H, complex multiplet),

1.60−0.90 (19H, complex multiplet), 0.90−0.75 (12H, overlapped doublets); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.7 (s, C-3), 110.5 (t, C-17), 75.0 (d, C-2), 65.6 (t, C-1), 39.4 (t), 37.4 (t), 37.3 (t), 37.2 (t), 36.8 (t), 33.0 (t), 32.8 (d), 32.7 (d), 28.0 (d), 25.5 (t), 24.8 (t), 24.5 (t), 22.7 (q), 22.6 (q), 19.7 (q, 2 × C); EIMS *m/z* 312 (2), 294 (0.2), 282 (2), 281 (9), 276 (0.3), 263 (7), 149 (10), 137 (16), 123 (31), 109 (46), 97 (48), 95 (65), 83 (67), 81 (62), 71 (69), 69 (100), 57 (73); HREIMS *m/z* $[M]^+$ 312.3025 (calcd for $C_{20}H_{40}O_2$ 312.3028).

Oxidation of Pseudoplexaurol (5). To a solution of pseudoplexaurol (32.5 mg, 0.11 mmol) in CH_2Cl_2 (10 mL) was added active 85% MnO_2 (150 mg, 1.5 mmol) and the mixture stirred at 25 °C for 7 h. The reaction product was filtered and then purified by column chromatography on silica gel (2 g) using 25% EtOAc in hexane to yield 9.8 mg of a colorless oil identical in all respects to pseudoplexaural (**4**).

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Supporting Information Available: Structures of known cembranoid diterpenes from *Eunicea*, recently discovered cembranolide diterpenes from *E. succinea*, and selected HREIMS fragment ions of compound **8** (3 pages). Ordering information is given on any current masthead page.

References and Notes

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(2) Presented in part at the 20th Senior Technical Meeting of the American Chemical Society, Puerto Rico Section, Tropimar Beach Club and Convention Center, Isla Verde, Puerto Rico, Nov 8−9, 1996.
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