Verticillane and Norverticillane Diterpenoids from the Formosan Soft Coral *Cespitularia hypotentaculata*

by **Jiun-Yang Chang**[a]), **Mohamed H. Abd El-Razek**[b]), and **Ya-Ching Shen***[b])

[a]) Department of Marine Biotechnology and Resources, National Sun Yat-Sen University, Kaohsiung 804, Taiwan, Republic of China

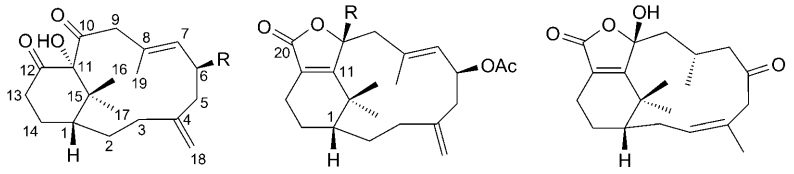
[b]) School of Pharmacy, College of Medicine, National Taiwan University, Jen-Ai Rd. Sec. 1, Taipei 100, Taiwan, Republic of China

(phone: +886-02-3123456, ext 62226; fax: +886-02-23919098; e-mail: ycshen@ntu.edu.tw)

Five new diterpenes, cespihypotins W–Z (**1**–**4**, resp.) and cespihypotone (**5**) have been isolated from the AcOEt-soluble fraction of the Formosan soft coral *Cespitularia hypotentaculata*. Two of them having the norverticillane skeleton, *i.e.*, **1** and **2**, and the other three, **3**–**5**, possessing a verticillane skeleton. The structures were established as (+)-(1βH,7*E*)-6β,11β-dihydroxynorverticilla-4(18),7-diene-10,12-dione (**1**), (+)-(1βH,7*E*)-6β-acetoxy-11β-hydroxynorverticilla-4(18),7-diene-10,12-dione (**2**), (−)-(1βH,7*E*)-6β-acetoxyverticilla-4(18),7,11-triene-10,12-γ-lactone (**3**), (+)-(1βH,7*E*)-6β-acetoxy-10-hydroxyverticilla-4(18),7,11-triene-10,12-γ-lactone (**4**), and (+)-(1βH,3*Z*)-10β-hydroxy-6-oxoverticilla-3,11-diene-10,12-γ-lactone (**5**), respectively, on the basis of 1D- and 2D-NMR spectroscopic analyses.

Introduction. – Verticillane diterpenoids have recently attracted the attention of natural product chemists due to their fundamental role in the biosynthesis of taxanes. It has been demonstrated that the cyclization mechanism from (*E*,*E*,*E*)-geranylgeranyl diphosphate to taxa-4,11-diene proceeds through a verticillen-12-yl carbocation intermediate [1]. Some hydroxylated verticillane derivatives have been isolated from diverse sources such as the conifer *Sciadopitys verticillata* [2], the dicotyledons *Bursera suntui* and *B. kerberi* [3], the soft coral *Cespitularia taeniata* [4], and the liverworts *Jackiella javanica* and *Jungermannia infusca* [5][6]. Several polyfunctionalized derivatives of this bicyclic diterpene have also been isolated from *Taxus* species. Taxuspine X possesses a potent multidrug-resistance reversing activity [7]. Soft corals of the genera *Cespitularia* and *Efflatounaria*, both belong to the family Xeniidae, do not retain their structural integrity on preservation in 70% alcohol, the former genus differs from the latter by having non-retractile polyps, which are often damaged on preservation; this makes taxonomy difficult. The soft corals of the genus *Cespitularia* have several color variants in the southern coast of Taiwan and have been found either as a potential source of bioactive compounds or a rich source of structurally unique and biologically active secondary metabolites, especially diterpenoids with a cembrane, neodolabellane, cespitularane, or verticillane skeleton [4]. Previous studies of the soft coral *C. hypotentaculata* ROXAS led to the isolation of diterpenoids with verticillane skeletons together with cespitularane contained 14-membered lactone ring between C(10) and C(12) [8–10]. In our continuing studies of the bioactive metabolites from the Formosan soft corals [11–13], five new diterpenes, **1**–**5**, have been isolated from

the AcOEt-soluble fraction of the Formosan soft coral *Cespitularia hypotentaculata*. Two of them having the norverticillane skeleton *i.e.*, **1** and **2**, and the other three, **3**–**5**, possessing a verticillane skeleton. Compounds **3**–**5** contain a γ-lactone ring between C(10) and C(12), which is also part of a 15-membered ring. The structures were established on the basis 1D- and 2D-NMR-spectroscopic analyses.



1 R = OH
2 R = AcO

3 R = H
4 R = OH

5

Results and Discussion. – A combination of column chromatography on silica gel and *Sephadex LH-20*, and preparative HPLC of the AcOEt-soluble portion of the Formosan soft coral *C. hypotentaculata* furnished five new verticillane diterpenes **1**–**5**.

Cespihypotin W (**1**) was isolated as a colorless amorphous solid. HR-EI-MS, ^{13}C-NMR, and DEPT spectra established the molecular formula of **1** as $C_{19}H_{28}O_4$. Thus, six degrees of unsaturation were determined for **1**. The IR absorptions at 3447, 1722, and 1652 cm^{-1} were attributed to OH and ketone groups. The presence of six sp^2 hybridized C-atoms in the molecule, as deduced from the ^{13}C-NMR and DEPT spectra (*Table 1*), corresponding to two C=C bonds, and two 1,3-dione C-atoms indicated compound **1** to be bicyclic. The ^{13}C-NMR *singlet* at δ(C) 133.1 and a *doublet* at δ(C) 132.0 that was correlated in the HMBC experiment with the ^{1}H-NMR signal at δ(H) 5.63 (*d*, $J = 9.3$, 1 H) together with the vinylic Me signals at δ(H) 1.84 (*s*) in the ^{1}H-NMR spectrum and at δ(C) 17.5 (*q*) in the ^{13}C-NMR spectrum were assigned to an (*E*)-trisubstituted C=C bond bearing a Me group [14]. The HMQC of δ(H) 4.85 (br. *s*, 1 H) and 4.95 (br. *s*, 1 H) with δ(C) 115.1 (*t*), as well as HMBC with δ(C) 144.5 (*s*), 38.8 (*t*), and 47.3 (*t*) indicated that **1** contained an exocyclic CH_2 group. HMQC of δ(H) 4.56 (*dt*, $J = 4.5$, 9.3, 1 H) with δ(C) 70.1 (*d*) and HMBC with δ(C) 133.1 (*s*) and 144.5 (*s*) supported that C(6)[1]) was hydroxylated. The geminal Me groups at δ(H) 1.50 (*s*) and 0.86 (*s*) showed HMBCs with δ(C) 46.5 (*s*), 43.3 (*d*), and the downfield tertiary alcohol C-atom at δ(C) 88.2 (*s*), which confirmed that **1** contained a gem-dimethyl bearing quaternary C-atom, which was adjacent to a CH C-atom, and a quaternary OH-bearing C-atom. The location of the oxo groups at C(10) and C(12) were assigned on the basis of the HMBCs of CH_2(9) with C(10) and of CH_2(13) with C(12). On the basis of the above data, the remaining two degrees of unsaturation suggested that compound **1** contains a bicyclic norverticillane ring similar to that previously reported for cespitularin M [10]. It was assumed that compound **1** was oxidized to a ketone at C(12) δ(C) 211.0 (*s*)), compared to the corresponding secondary alcohol group (δ(H) 4.10, *m*, H–C(12) and δ(C) 77.5 (*d*)) in cespitularin M. The relative configuration of **1** was determined by analysis of NOESY correlations. We assume that **1** has the same absolute configuration at C(1) as other naturally occurring cespitularines and taxoids

[1]) Arbitrary numbering. For systematic names, see *Exper. Part.*

[15]. A NOESY experiment was performed to ascertain the relative configuration of C(11), Me(16), Me(17), and C(6) (*Fig. 1*). The presence of mutual correlations between H–C(1) and Me(16) and Me(17) agreed with β-configurations for these groups, while H–C(6) had α-configuration. The β-configuration of the OH group at C(6) was confirmed by comparison of the previously reported norditerpenoid cespihypotin A [8]. Meanwhile, the broad *singlet* of the OH group attached to C(11) showed a NOESY correlation with the α-H-atom at δ(H) 2.93–2.96 of C(13), and comparison with cespitularin M [10] confirmed the OH group should have an α-orientation. Taking all these spectroscopic data into account, compound **1** was elucidated as (+)-(1βH,7*E*)-6β,11β-dihydroxynorverticilla-4(18),7-diene-10,12-dione.

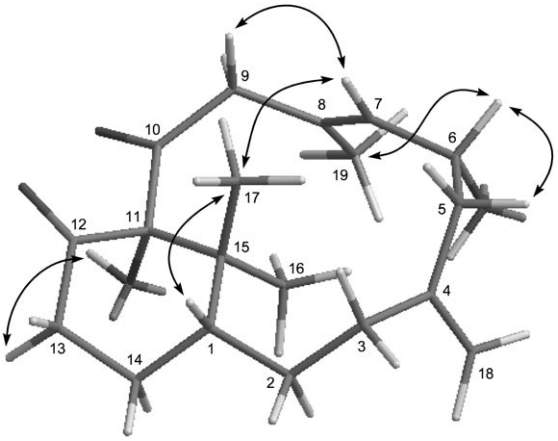


Fig. 1. *Computer-generated perspective model for* **1** *using MM2 force field calculations and NOESY correlations*

Cespihypotin X (**2**) gave a formula of $C_{21}H_{30}O_5$, from the interpretation of its HR-ESI-MS and ^{13}C-NMR data. The NMR features (*Tables 1* and *2*) of **2** were analogous to those of **1** with the exception that the resonances for the secondary OH at C(6)[1]) were replaced by those of an AcO group. The COSY correlations from H–C(6) to H–C(5) and H–C(7), and the HMBC correlations from H–C(6) to C(5), C(7), C(8), and the CO C-atom of AcO–C(6) suggested these assignments. Thus, **2** was determined as (+)-(1βH,7*E*)-6β-acetoxy-11β-hydroxynorverticilla-4(18),7-diene-10,12-dione.

Cespihypotin Y (**3**) possesses the molecular formula $C_{22}H_{30}O_4$, as deduced from the HR-ESI-MS and ^{13}C-NMR spectroscopic data, indicating eight degrees of unsaturation. The UV and IR spectra of **3** showed the presence of α,β-unsaturated γ-lactone and CO ester functionalities, respectively. The ^{1}H-NMR spectrum (*Table 1*) of **3** exhibited characteristic signals including a *doublet* at δ(H) 5.37 (*d*, *J* = 8.0, 1 H), two *singlet*s at δ(H) 4.81 (*s*, 1 H) and 4.79 (*s*, 1 H), a broad *singlet* at δ(H) 5.23, and a *doublet* of *triplet*s at δ(H) 5.33 (*dt*, *J* = 2.5, 8.0, 1 H). The ^{13}C-NMR spectrum (*Table 2*) of **3** showed signals of a conjugated ester C-atom (δ(C) 172.9), three Me C-atoms (δ(C) 34.2, 24.8, 18.1), and one quaternary C-atom at δ(C) 36.6 (C(15)[1])). The H- and C-atom

Table 1. *^{1}H-NMR Data* (δ in ppm, J in Hz, 300 MHz, in $CDCl_3$) *of Compounds* **1**–**5**

Position	**1**	**2**	**3**	**4**	**5**
1	1.45 (br. *s*)	1.44 (br. *s*)	1.74–1.78 (*m*)	1.67–1.73 (*m*)	1.75–1.80 (*m*)
2	1.22–1.28 (*m*)	1.83–1.87 (*m*), 1.23–1.29 (*m*)	2.20–2.25 (*m*), 2.34 (*dd*, *J* = 3.0, 9.0)	2.40–2.46 (*m*)	1.97–2.03 (*m*), 2.45–2.50 (*m*)
3	1.93 (*t*, *J* = 13.8), 2.35–2.40 (*m*)	1.85 (*t*, *J* = 13.8), 2.32–2.37 (*m*)	2.02–2.07 (*m*), 2.28 (br. *d*, *J* = 9.0)	2.02–2.06 (*m*), 2.20–2.24 (*m*)	5.43 (*d*, *J* = 12.0)
5	2.13–2.19 (*m*), 2.72 (*dd*, *J* = 4.5, 11.8)	2.12–2.18 (*m*), 2.80 (*dd*, *J* = 4.5, 11.8)	2.22–2.38 (*m*), 2.44 (*dd*, *J* = 8.0, 13.0)	2.42–2.48 (*m*), 2.80–2.84 (*m*)	2.48 (*d*, *J* = 16.0), 3.68 (*d*, *J* = 16.0)
6	4.56 (*dt*, *J* = 4.5, 9.3)	5.51 (*dt*, *J* = 3.0, 9.6)	5.33 (*dt*, *J* = 2.5, 8.0)	5.32 (*dt*, *J* = 2.1, 8.1)	
7	5.63 (*d*, *J* = 9.3)	5.57 (*d*, *J* = 9.6)	5.37 (*d*, *J* = 8.0)	5.42 (*d*, *J* = 8.4)	2.20–2.24 (*m*)
8	–	–	–	–	1.74–1.80 (*m*)
9	2.93 (br. *d*, *J* = 12.9), 3.78 (*d*, *J* = 12.9)	2.92 (*d*, *J* = 12.0), 3.77 (*d*, *J* = 12.0)	2.70 (*dd*, *J* = 15.0, 3.5), 2.95 (*dd*, *J* = 15.0, 3.5)	2.97 (*AB*, *J* = 13.8)	1.93–1.98 (*m*)
10			5.23 (br. *s*)		
13	2.50 (*dd*, *J* = 3.0, 15.0), 2.90–2.96 (*m*)	2.56 (*dd*, *J* = 4.0, 15.0), 2.88–2.93 (*m*)	1.73–1.78 (*m*), 2.18–2.24 (*m*)	1.75–1.80 (*m*), 2.19–2.23 (*m*)	1.61–1.67 (*m*), 2.20–2.24 (*m*)
14	1.67–1.73 (*m*), 2.13–2.18 (*m*)	1.02–1.08 (*m*), 1.67–1.73 (*m*)	1.50–1.54 (*m*), 1.65–1.70 (*m*)	1.45–1.50 (*m*), 1.57–1.63 (*m*)	2.42–2.48 (*m*)
16	0.86 (*s*)	0.86 (*s*)	1.20 (*s*)	1.26 (*s*)	1.24 (*s*)
17	1.50 (*s*)	1.50 (*s*)	1.39 (*s*)	1.46 (*s*)	1.30 (*s*)
18	4.85 (br. *s*), 4.95 (br. *s*)	4.92 (*s*), 5.03 (*s*)	4.81 (*s*), 4.79 (*s*)	4.81 (*s*), 4.79 (*s*)	1.72 (*s*)
19	1.84 (*s*)	1.90 (*s*)	1.64 (*s*)	1.84 (*s*)	1.80 (*d*, *J* = 7.0)
11-OH	4.17 (*s*)	4.17 (*s*)			
Ac		2.04 (*s*)	2.02 (*s*)	2.02 (*s*)	

Table 2. *^{13}C-NMR Data* (δ in ppm, 75 MHz, $CDCl_3$) *of Compounds* **1**–**5**[a])

Position	**1**	**2**	**3**	**4**	**5**
1	43.3 (*d*)	43.3 (*d*)	42.5 (*d*)	43.5 (*d*)	43.4 (*d*)
2	34.3 (*t*)	34.5 (*t*)	18.3 (*t*)	18.1 (*t*)	16.6 (*t*)
3	38.3 (*t*)	38.7 (*t*)	31.4 (*t*)	32.2 (*t*)	129.7 (*d*)
4	144.5 (*s*)	143.9 (*s*)	145.3 (*s*)	145.4 (*s*)	146.9 (*s*)
5	47.3 (*t*)	44.2 (*t*)	40.5 (*t*)	40.6 (*t*)	44.1 (*t*)
6	70.1 (*d*)	72.3 (*d*)	71.3 (*d*)	71.4 (*d*)	209.0 (*s*)
7	132.0 (*d*)	127.3 (*d*)	130.1 (*d*)	131.6 (*d*)	51.6 (*t*)
8	133.1 (*s*)	135.0 (*s*)	135.2 (*s*)	133.3 (*s*)	26.7 (*d*)
9	48.5 (*t*)	48.5 (*t*)	42.2 (*t*)	48.5 (*t*)	43.3 (*t*)
10	206.0 (*s*)	206.1 (*s*)	81.8 (*s*)	109.0 (*s*)	109.1 (*s*)
11	88.2 (*s*)	88.2 (*s*)	169.8 (*s*)	168.1 (*s*)	166.0 (*s*)
12	211.0 (*s*)	210.8 (*s*)	127.1 (*s*)	129.0 (*s*)	128.3 (*s*)
13	35.8 (*t*)	35.8 (*t*)	23.7 (*t*)	23.7 (*t*)	25.2 (*t*)
14	29.3 (*t*)	29.2 (*t*)	31.5 (*t*)	31.8 (*t*)	32.3 (*t*)
15	46.5 (*s*)	46.5 (*s*)	36.6 (*s*)	37.0 (*s*)	38.3 (*s*)
16	24.5 (*q*)	24.5 (*q*)	24.8 (*q*)	24.1 (*q*)	24.3 (*q*)
17	26.0 (*q*)	25.9 (*q*)	34.2 (*q*)	33.9 (*q*)	38.3 (*q*)
18	115.1 (*t*)	115.7 (*t*)	114.0 (*t*)	114.5 (*t*)	24.5 (*q*)
19	17.5 (*q*)	17.6 (*q*)	18.1 (*q*)	17.1 (*q*)	22.6 (*q*)
20			172.9 (*s*)	170.9 (*s*)	170.4 (*s*)
AcO		170.2 (*s*), 21.2 (*q*)	169.9 (*s*), 21.2 (*q*)	170.2 (*s*), 21.3 (*q*)	

[a]) Assignments were aided by HMBC and DEPT techniques.

assignments were determined by COSY, HMQC, and HMBC. Detailed comparison of the ^{1}H- and ^{13}C-NMR data (*Tables 1* and *2*) with those of cespitularin O [10] revealed that compound **3** is a 6-AcO analogue of cespitularin O. A COSY correlation from CH_2(9) to H–C(10) and HMBC from CH_2(9) to C(7), C(10), C(11), and C(19) helped to ascertain this assignment. NOESY correlations of Me(17)/H–C(10), Me(19)/H–C(6), and Me(17)/H–C(7) indicated Me(16), Me(17), H–C(7), AcO–C(6), and H–C(10) were on the same side of the molecule. Thus, from these data, the structure of **3** was established as (–)-(1βH,7*E*)-6β-acetoxyverticilla-4(18),7,11-triene-10,12-γ-lactone.

Cespihypotin Z (**4**) proved to have the molecular formula $C_{22}H_{30}O_5$ from the HR-ESI-MS and ^{13}C-NMR spectroscopic data. The NMR features (*Tables 1* and *2*) of **4** showed some similarity to those of compound **3** except for the replacement of the secondary OH group at C(10)[1]) by a tertiary alcoholic C-atom in **4**. Analyses of 2D-NMR data revealed that **4** possessed the same carbocyclic skeleton as **3**. However, there was a significant difference that indicated the presence of a γ-hydroxy-α,β-unsaturated-γ-lactone (δ(C) 170.9 (*s*), 129.0 (*s*), 168.1 (*s*), 109.0 (*s*)) in **4** instead of a γ-hydroxymethine-α,β-unsaturated-γ-lactone (δ(C) 172.9 (*s*), 127.1 (*s*), 169.8 (*s*), 81.8 (*d*)) in **3**. HMBCs between Me(16), Me(17) and C(11); CH_2(13) and C(14), C(1), C(20); CH_2(9) and C(10), C(11), C(8), C(7), C(19); and Me(19) and C(7), C(8), C(9) clearly positioned the γ-hydroxy-α,β-unsaturated-γ-lactone. The relative configuration of **4** was deduced from a 2D-NOESY experiment, which indicated that Me(16),

Me(17), H–C(7), and H–C(1) are on one side of the molecule, while Me(19) and H–C(6) are on the opposite side of the molecule (*Fig. 2*).

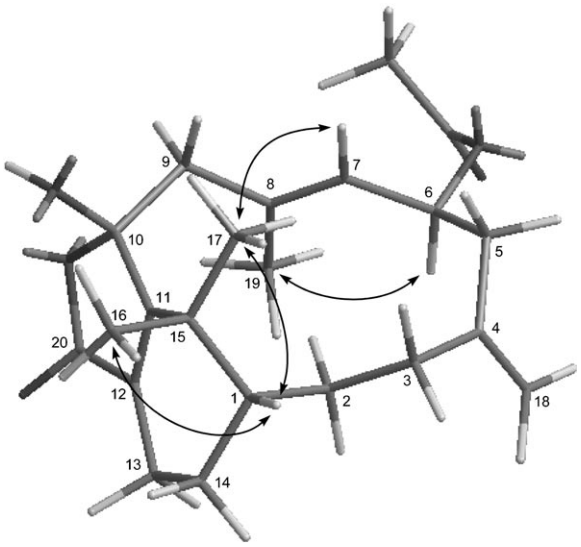


Fig. 2. *Computer-generated perspective model for* **4** *using MM2 force field calculations and NOESY correlations*

Cespihypotone (**5**) has the molecular formula, $C_{20}H_{28}O_4$, as determined by HR-ESI-MS and NMR spectra (*Tables 1* and *2*). The IR spectrum of **5** indicated the presence of a OH group at 3420 cm^{-1} and ketones at 1740 and 1705 cm^{-1}. The UV absorption at λ_{max} 235 nm suggested the presence of an α,β-unsaturated ketone. The NMR features of compound **5** were analogous to those of compound **4** except that the O-bearing CH_2 group at C(4)[1]) and the olefinic Me at C(8) in **4** were replaced by a *cis* olefinic Me (δ(H) 1.72 *s*; δ(C) 24.5 *q*), a secondary Me (δ(H) 1.80, *d*, $J = 7.0$; δ(C) 22.6 *q*), and keto group at C(6) (δ(C) 209.0 *s*) respectively. The relative configuration of **5** was deduced from a NOESY experiment, which indicated that Me(16), Me(17), H–C(8β), and H–C(1) are on one side of the molecule. The NOESY between Me(18) and H–C(3) confirmed the (*Z*)-configuration at C(3)=C(4) (*Fig. 3*). Detailed analyses of the 1D- and 2D-NMR spectra led us assign the structure of **5** as (+)-(1βH,3*Z*)-10β-hydroxy-6-oxoverticilla-3,11-diene-10,12-γ-lactone.

A plausible biogenetic pathway to compounds **1** and **2** is proposed as illustrated in the *Scheme* based on recently published verticillanes [11][12]. Analogs of the precursor **a**, which have been recently isolated from *C. hypotenculata* [9][11] are quite significant from a biogentic point of view. The nor-verticillanes **1** and **2** may be produced through decarboxyaltion, expoxidation, and hydration of precursor **a**. The biogentic pathway for compounds **3**–**5** may refer to a proposed scheme published in a previous paper [12].

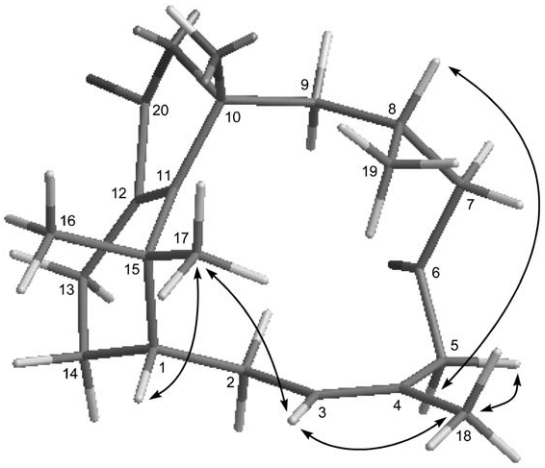
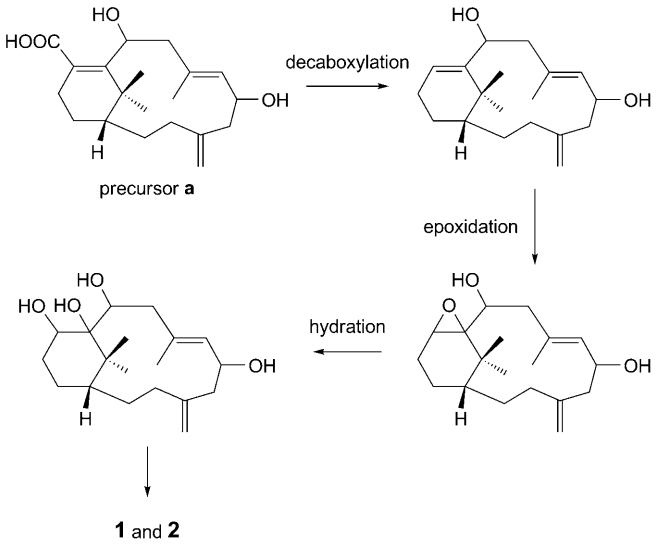


Fig. 3. *Computer-generated perspective model for* **5** *using MM2 force field calculations and NOESY correlations*

Scheme. *Biogenetic Pathway to Compounds* **1** *and* **2**



Experimental Part

General. Column chromatography (CC): silica gel *60* (SiO_2; *Merck*) and *Sephadex LH-20* (*Amersham Pharmacia Biotech AB*, Uppsala, Sweden); FC = flash chromatography. Prep. TLC: precoated SiO_2 plates (*Merck*; silica gel *60 F-254*, 1 mm). Optical rotations: *Jasco DIP-1000* polarimeter. UV Spectra: *Hitachi U-3210* spectrometer; λ_{max} (log ε) in nm. IR Spectra : *Hitachi T-2001* spectrometer; in cm^{-1}. ^1H- and ^{13}C-NMR, COSY, HMQC, HMBC, and NOESY Experiments: *Bruker FT-300*

spectrometer or *Varian Unity-Inova-500* FT-NMR spectrometers at 500 (^{1}H) and 125 MHz (^{13}C), Me_4Si as internal standard; δ in ppm, coupling constants J in Hz. EI-MS and FAB-MS: VG *Quattro 5022* mass spectrometer; in *m/z* (rel. %).

Animal Material. The soft coral *C. hypotentaculata* ROXAS (Xeniidae) was collected at Green island, off the eastern coast of Taiwan, in December 2004, by scuba diving at a depth of 15 m. The fresh coral was immediately frozen after collection and kept at $-20°$ until processed. A voucher specimen (NTUO-5) was deposited in the School of Pharmacy, College of Medicine, National Taiwan University, Taiwan.

Extraction and Isolation. The soft coral (wet, 8 kg) was extracted with CH_2Cl_2/MeOH (1:1, 3×10 l) at r.t. and the extract was concentrated under vacuum. The crude extract (20 g) was partitioned between AcOEt and H_2O (1:1). The AcOEt soluble portion was subjected to FC SiO_2, hexane/AcOEt (100:0/0:100). The fraction eluted with hexane/AcOEt 4:1 was separated on *Sephadex LH-20* using CH_2Cl_2/MeOH (1:1) to furnish five fractions (*F1*–*F5*). This was followed by fractionation of *F5* (1.3 g) by SiO_2 CC eluting gradiently with hexane/CH_2Cl_2/MeOH 100:0:0–0:3:1 to give seven fractions (*F5-1*–*F5-7*). *F5-3* was further subjected to separation on NP-HPLC using hexane/AcOEt 7:3 to yield **2** (7 mg), and **3** (2 mg). While *F5-5* was separated on NP-HPLC using hexane/AcOEt 5:3 to give **1** (6 mg) and **4** (6 mg). *F5-7* was chromatographed on NP-HPLC eluted with hexane/AcOEt (3:2) to afford **5** (5 mg).

Cespihypotin W (=*(1*R*,4*E*,6*S*,11*R*)-1,6-Dihydroxy-4,15,15-trimethyl-8-methylidenebicyclo[9.3.1]-pentadec-4-ene-2,14-dione*; **1**). Colorless amorphous solid. $[\alpha]_D^{25} = +49.4$ ($c = 0.6$, CH_2Cl_2). UV (MeOH): 207 (3.18). IR (neat): 3447, 2924, 1722, 1652. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS: 343.1885 ($C_{19}H_{28}NaO_4^+$; 343.1884).

Cespihypotin X (=*(1*R*,4*E*,6*S*,11*R*)-1-Hydroxy-4,15,15-trimethyl-8-methylidene-2,14-dioxobicyclo[9.3.1]pentadec-4-en-6-yl Acetate*; **2**). Colorless amorphous solid. $[\alpha]_D^{25} = +64.4$ ($c = 0.6$, CH_2Cl_2). UV (MeOH): 206 (3.31). IR (neat): 3445, 2926, 1720, 1650. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS: 385.1987 ($C_{21}H_{30}NaO_5^+$; calc. 385.1991).

Cespihypotin Y (=*(5*R*,10*S*,11*E*,13a*R*)-2,4,5,6,7,8,9,10,13,13a-Decahydro-4,4,12-trimethyl-8-methylidene-2-oxo-3,5-ethanocyclododeca[*b*]furan-10-yl Acetate*; **3**). Colorless amorphous solid. $[\alpha]_D^{25} = -112.2$ ($c = 0.6$, CH_2Cl_2). UV (MeOH): 208 (3.27), 247 (3.33). IR (neat): 2940, 1720, 1654. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS: 381.2042 ($C_{22}H_{30}NaO_4^+$; calc. 381.2040).

Cespihypotin Z (=*(5*R*,10*S*,11*E*,13a*R*)-2,4,5,6,7,8,9,10,13,13a-Decahydro-13a-hydroxy-4,4,12-trimethyl-8-methylidene-2-oxo-3,5-ethanocyclododeca[*b*]furan-10-yl Acetate*; **4**). Colorless amorphous solid. $[\alpha]_D^{25} = +86.4$ ($c = 0.6$, CH_2Cl_2). UV (MeOH): 210 (3.23), 245 (3.21). IR (neat): 3410, 2945, 1734, 1652. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS: 397.1991 ($C_{22}H_{30}NaO_5^+$; calc. 397.1989).

Cespihypotone (=*(5*S*,7*Z*,12*S*,13a*R*)-4,5,6,9,11,12,13,13a-Octahydro-13a-hydroxy-4,4,8,12-tetramethyl-3,5-ethanocyclododeca[*b*]furan-2,10-dione*; **5**). Colorless amorphous solid. $[\alpha]_D^{25} = +68$ ($c = 0.6$, CH_2Cl_2). UV (MeOH): 207 (3.30), 235 (3.21). IR (neat): 3420, 2950, 1740, 1705, 1650. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: *Table 2*. HR-ESI-MS: 355.1885 ($C_{20}H_{28}NaO_4^+$; calc. 355.1883).

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