Verticillane-Type Diterpenoids and an Eudesmanolide-Type Sesquiterpene from the Formosan Soft Coral *Cespitularia hypotentaculata*

by **Yu-Chi Lin**[a])[b]), **Mohamed H. Abd El-Razek**[a]), and **Ya-Ching Shen***[a])

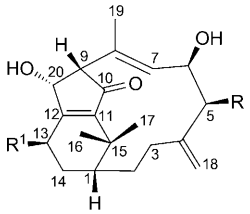
[a]) School of Pharmacy, College of Medicine, National Taiwan University, Taipei 100, Taiwan, R.O.C. (phone: +886-2-23123456 ext. 62226; fax: +886-02-23919098; e-mail: ycshen@ntu.edu.tw)
[b]) Department of Marine Biotechnology and Resources, National Sun Yat-Sen University, Kaohsiung 804, Taiwan, R.O.C.

Four new diterpenes, cespihypotins W–Z (**1**–**4**), having the verticillane skeleton and characterized by an α,β-unsaturated γ-hydroxycyclopentanone moiety, and a new eudesmanolide-type sesquiterpene, cespilactam A (**5**), containing an α,β-unsaturated γ-lactam residue, were isolated from the AcOEt-soluble fraction of the Taiwanese soft coral *Cespitularia hypotentaculata*. The structure and relative configuration of these metabolites was elucidated through extensive interpretation of MS, COSY, HSQC, HMBC, and NOESY experiments and by comparison of their NMR data with those of related compounds.

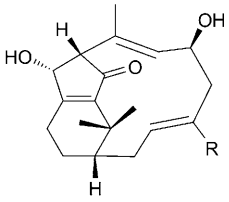
Introduction. – Marine terpenoids are of particular interest owing to their varied and pronounced biological activities as well as their unique C-atom skeletons. Soft corals (phylum Cnidaria, class Anthozoa, subclass Octocorallia, order Alcyonacea, family Xeniidae, genus *Cespitularia*) have proven to be a rich source of diterpenoids with cembrane, neodolabellane, verticillane, norverticillane, and cespitularane skeletons, and some of these compounds demonstrated cytotoxic activities [1–11]. Cembranoid diterpenes are quite common in soft corals, particularly in the genus *Sarcophyton* [12]. The cespihyptins are diterpenes with a core bicyclo[9.3.1]pentadecane ring system. This ring system has close congruence with the 'verticillane' C-atom framework. Although verticillanes are relatively rare in nature, verticillol was isolated from an evergreen wood of the conifer *Sciadopitys vertilillata* [13]. Its enantiomer and the corresponding hydrocarbons were found in the Japanese liverwort *Jackiella javanica* [14]. The essential oil of *Boswellia carterii* contains verticilla-4(20),7,11-triene [15]. Up to now, about 30 verticillane- and norverticillane-type diterpenoids have been reported from the Formosan soft coral of the genus *Cespitularia* [5][6][8–10]. Recently, eleven new N-containing verticillane diterpenes have been isolated from the Taiwanese soft coral *Cespitularia taeniata* [7][11]. In the course of our ongoing studies on marine natural products, we have recently examined the MeOH extract of the soft coral collected off the coast in southern Taiwan, identified as *Cespitularia hypotentaculatam*, and have isolated four new diterpenes, cespihypotins W–Z[1]) (**1**–**4**), having the verticillane skeleton and characterized by an α,β-unsaturated γ-hydroxycyclopen-

[1]) Trivial atom numbering; for systematic names, see *Exper. Part.*

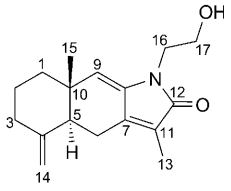
tanone moiety. Their structures were established as (+)-(1*β*,5*β*,6*β*,7*E*,9*β*,20*α*)-5,6,20-trihydroxyverticilla-4(18),7,11-trien-10-one (**1**), (−)-(1*β*,3*Z*,6*β*,7*E*,9*β*,20*α*)-6,18,20-trihydroxyverticilla-3,7,11-trien-10-one (**2**), (−)-(1*β*,3*Z*,6*β*,7*E*,9*β*,20*α*)-6,20-dihydroxy-10-oxoverticilla-3,7,11-trien-18-al (**3**), and (+)-(1*β*,6*β*,7*E*,9*β*,13*β*,20*α*)-6,13,20-trihydroxyverticilla-4(18),7,11-trien-10-one (**4**). Moreover, a new eudesmanolide-type sesquiterpene with an *α*,*β*-unsaturated *N*-alkyl-*γ*-lactam structure was isolated and designated as cespilactam A[1]) (**5**). The details of characterization and structure elucidation of these five new secondary metabolites are discussed below. To the best of our knowledge, this is the first report of OH substitution in ring *A* of a verticillane-type diterpenoid (see **4**), and compound **5** is proposed to be the first *N*-alkyl-substituted eudesmanolide-type sesquiterpene from the family Xeniidae.



1[1]) R = OH, R^1 = H
4[1]) R = H, R^1 = OH



2 R = $HOCH_2$
3 R = CHO



5[1])

Results and Discussion. – The minced bodies of *Cespitularia hypotentaculata* were exhaustively extracted with CH_2Cl_2/EtOH 1:1, and the concentrated extract was fractionated by column chromatography (silica gel, hexane, hexane/AcOEt mixtures of increasing polarity, then AcOEt/MeOH with different ratios). The eluted fractions were further purified by various chromatographic techniques including gel permeation and HPLC to afford **1**–**5** (see *Exper. Part*).

Cespihypotins W (**1**), X (**2**), and Z (**4**) were assigned the same formula $C_{20}H_{28}O_4$, whereas cespihypotin Y (**3**) had the molecular formula $C_{20}H_{26}O_4$ as derived from HR-ESI-MS, ^{13}C-NMR, and DEPT data. Thus, seven degrees of unsaturation were determined for **1**, **2**, and **4** and eight degrees of unsaturation for **3**. The ^{1}H- and ^{13}C-NMR data of cespihypotins W–Z (**1**–**4**) (*Tables 1* and *2*) were similar to each other and to those of cespitularin F (=(1*R*,2*S*,5*R*,12*S*,13*E*)-1,2,4,5,6,7-hexahydro-1,12-dihydroxy-4,4,14-trimethyl-10-methylene-2,5-hept[1]eno-3*H*-inden-3-one) [6], isolated previously from *Cespitularia hypotentaculata*. The differences reflected varying substitutions and varying positions of the C=C bond inside the skeleton. The ^{1}H-NMR spectra of **1**–**4** showed three Me *s*, and the ^{13}C-NMR spectra revealed 20 C-atom signals in all cases, except for their side chains. The IR spectrum showed the presence of OH groups (3385 (**1**), 3376 (**2**), 3394 (**3**), and 3416 cm^{-1} (**4**)) and an *α*,*β*-unsaturated C=O group (1689 (**1**), 1692 (**2**), 1697 (**3**), and 1695 cm^{-1} (**4**)). The UV absorption at λ_{max} 234 (**1**), 236 (**2**), 238 (**3**), and 232 nm (**4**) also suggested the presence of an *α*,*β*-unsaturated C=O group.

Cespihypotin W (**1**) was isolated as an optically active colorless amorphous solid. The presence of seven sp^2-hybridized C-atoms in the molecule, as deduced from the ^{13}C-NMR and DEPT spectra (*Table 2*), corresponding to a tetrasubstituted C=C bond, a trisubstituted C=C bond, an exocyclic CH_2=C moiety, and an *α*,*β*-unsaturated C=O

Table 1. *^{1}H-NMR Data* (500 MHz, $CDCl_3$) of *Compounds* **1**–**5**[a])

	1	**2**	**3**	**4**	**5**
H–C(1) or CH_2(1)	1.70 (br. *s*)	1.75–1.79 (*m*)	1.90 (br. *s*)	1.86–1.92 (*m*)	1.52–1.68 (*m*)
CH_2(2)	1.79–1.83 (*m*), 1.80–1.86 (*m*)	2.00–2.04 (*m*), 2.91–2.97 (*m*)	2.29 (*d*, *J* = 13.6), 3.86 (*dt*, *J* = 10.4, 2.4)	1.67–1.74 (*m*), 2.07–2.13 (*m*)	1.67–1.73 (*m*)
CH_2(3) or H–C(3)	1.96–2.02 (*m*), 2.15 (*dd*, *J* = 16.0, 10.0)	5.10 (*d*, *J* = 16.2)	6.39 (*d*, *J* = 13.6)	2.46 (*dd*, *J* = 18.3, 8.1), 1.92–1.98 (*m*)	1.98–2.03 (*m*), 2.34 (*d*, *J* = 1.6)
H–C(5) or CH_2(5)	4.35 (*d*, *J* = 5.0)	2.00–2.04 (*m*), 2.57–2.63 (*m*)	1.90–1.94 (*m*), 2.93 (*d*, *J* = 13.6)	1.92 (*dd*, *J* = 13.5, 3.3), 2.53 (*dd*, *J* = 13.2, 3.6)	2.27 (*d*, *J* = 13.2)
H–C(6) or CH_2(6)	4.58 (*dd*, *J* = 10.0, 5.0)	4.58 (*d*, *J* = 10.2)	4.56 (*dd*, *J* = 9.2, 6.6)	4.56 (*ddd*, *J* = 9.5, 3.6, 3.3)	2.43 (*t*, *J* = 13.2), 2.62 (*dd*, *J* = 13.2, 3.6)
H–C(7)	4.69 (*d*, *J* = 10.0)	5.14 (*d*, *J* = 10.2)	4.78 (*d*, *J* = 9.2)	4.87 (*d*, *J* = 9.5)	
H–C(9)	3.30 (*d*, *J* = 5.5)	3.22 (*d*, *J* = 6.0)	3.35 (*d*, *J* = 6.4)	3.35 (*d*, *J* = 5.7)	5.40 (*s*)
CH_2(13), H–C(13), or Me(13)	2.30–2.36 (*m*), 1.84–1.90 (*m*)	2.72–2.78 (*m*), 2.39–2.43 (*m*)	2.76 (*d*, *J* = 9.6), 2.46 (*d*, *J* = 8.0)	4.81–4.86 (*m*)	1.85 (*s*)
CH_2(14)	2.25–2.30 (*m*), 2.77 (*dd*, *J* = 12.0, 2.5)	1.87–1.93 (*m*), 2.30–2.34 (*m*)	1.96–2.02 (*m*), 2.33–2.39 (*m*)	2.21–2.27 (*m*)	4.86 (*s*), 4.61(*s*)
Me(15)					0.89 (*s*)
Me(16) or CH_2(16)	1.15 (*s*)	1.16 (*s*)	1.17 (*s*)	1.24 (*s*)	3.68 (*t*, *J* = 4.4)
Me(17) or CH_2(17)	1.37 (*s*)	1.44 (*s*)	1.41 (*s*)	1.32 (*s*)	3.76 (*t*, *J* = 4.4)
CH_2(18) or H–C(18)	4.79 (*s*), 5.01 (*s*)	3.80 (*d*, *J* = 12.3), 4.41 (*d*, *J* = 12.3)	10.12 (*s*)	4.98 (br. *s*)	
Me(19)	1.88 (*s*)	1.86 (*s*)	1.82 (*s*)	1.85 (*s*)	
H–C(20)	4.82 (*d*, *J* = 5.5)	4.84 (*d*, *J* = 5.7)	4.79 (*d*, *J* = 6.4)	5.15 (*d*, *J* = 5.7)	

[a]) Assignments were established by COSY, HSQC, NOESY, and HMBC experiments; *J* values in Hz.

Table 2. *^{13}C-NMR Data* (125 MHz, $CDCl_3$) *of Compounds* **1**–**5**[a]). δ in ppm.

	1	**2**	**3**	**4**	**5**
C(1)	41.4 (*d*)	42.8 (*d*)	44.2 (*d*)	45.3 (*d*)	39.4 (*t*)
C(2)	25.3 (*t*)	33.7 (*t*)	33.7 (*t*)	27.5 (*t*)	23.2 (*t*)
C(3)	24.3 (*t*)	132.6 (*d*)	154.9 (*d*)	31.7 (*t*)	36.2 (*t*)
C(4)	147.7 (*s*)	133.0 (*s*)	136.9 (*s*)	145.0 (*s*)	148.6 (*s*)
C(5)	78.7 (*d*)	44.7 (*t*)	39.4 (*t*)	45.6 (*t*)	48.9 (*d*)
C(6)	70.5 (*d*)	70.0 (*d*)	67.5 (*d*)	66.9 (*d*)	22.2 (*t*)
C(7)	127.1 (*d*)	132.5 (*d*)	132.1 (*d*)	132.4 (*d*)	140.1 (*s*)
C(8)	138.1 (*s*)	134.8 (*s*)	136.3 (*s*)	133.6 (*s*)	137.5 (*s*)
C(9)	61.1 (*d*)	61.6 (*d*)	63.8 (*d*)	63.4 (*d*)	119.7 (*d*)
C(10)	204.0 (*s*)	204.5 (*s*)	207.0 (*s*)	204.7 (*s*)	38.0 (*s*)
C(11)	147.7 (*s*)	147.2 (*s*)	148.0 (*s*)	148.4 (*s*)	124.2 (*s*)
C(12)	170.3 (*s*)	167.1 (*s*)	171.0 (*s*)	165.8 (*s*)	172.4 (*s*)
C(13)	21.6 (*t*)	22.9 (*t*)	23.6 (*t*)	63.7 (*t*)	8.4 (*q*)
C(14)	21.8 (*t*)	24.9 (*t*)	25.8 (*t*)	34.3 (*t*)	107.2 (*t*)
C(15)	34.2 (*s*)	33.5 (*s*)	35.0 (*s*)	33.9 (*s*)	16.3 (*q*)
C(16)	24.3 (*q*)	30.7 (*q*)	30.9 (*q*)	30.8 (*q*)	42.8 (*t*)
C(17)	30.0 (*q*)	21.7 (*q*)	22.3 (*q*)	23.6 (*q*)	61.9 (*t*)
C(18)	112.2 (*t*)	60.3 (*t*)	194.1 (*s*)	112.2 (*q*)	
C(19)	20.8 (*q*)	19.8 (*q*)	19.6 (*q*)	19.4 (*q*)	
C(20)	72.8 (*d*)	73.9 (*d*)	74.2 (*d*)	72.2 (*d*)	

[a]) Assignments were established by HMBC and DEPT experiments.

group indicated that **1** possesses a tricyclic skeleton. The ^{13}C-NMR *s* at δ(C) 138.1 (C(8)) and a *d* at δ(C) 127.1 (C(7)) that was correlated in the HMBC experiment with the ^{1}H-NMR signal at δ(H) 4.69 (*d*, $J = 10.0$ Hz, H–C(7)), together with the olefinic-Me signal at δ(H) 1.88 (*s*, Me(19)) and δ(C) 20.8 (*q*) were assigned to an (*E*)-trisubstituted C=C bond bearing a Me group [6]. The ^{13}C-NMR spectrum revealed the presence of an α,β-unsaturated C=O group (δ(C) 204.0 (C(10)), 147.7 (C(11)), and 170.3 (C(12)), which was verified by COSY and HMBC data. The COSY cross-peak H–C(20)/H–C(9) and the HMBCs H–C(20)/C(8) and C(11) implied that the OH group should be at C(20). Furthermore, the HMBCs H–C(9)/C(7), C(8), C(10), C(11), C(12), and C(20), H–C(20)/C(8), C(11), and C(12), CH_2(13)/C(12), and Me(16)/C(1) and C(11) accounted for the presence of an α,β-unsaturated γ-hydroxycyclopentanone moiety. The HMQC cross-peak of δ(H) 4.97 (*s*, 1 H–C(18)) and 5.01 (*s*, 1 H–C(18)) with δ(C) 112.2 (*t*, C(18)), as well as the HMBC with δ(C) 147.7 (*s*, C(4)), 24.3 (*t*, C(3)), and 78.7 (*d*, C(5)) indicated that **1** contained an exocyclic CH_2 group at C(4). A HMQC cross-peak of δ(H) 4.58 (*dd*, $J = 10.0$, 5.0 Hz, H–C(6)) with δ(C) 70.5 (*d*, C(6)) and a HMBC with δ(C) 138.1 (*s*, C(8)) and 147.7 (*s*, C(4)) demonstrated that C(6) is hydroxylated. The geminal Me groups at δ(H) 1.15 and 1.37 (2*s*, Me(16) and Me(17)) showed HMBCs with δ(C) 34.2 (*s*, C(15)) and 41.4 (*d*, C(1)) confirming that **1** has a dimethyl-bearing quaternary C-atom which is adjacent to CH(1). On the basis of the above data, it was suggested that compound **1** contains a tricyclic verticillane ring similar to that reported previously for cespitularin F [6], except for the CH_2(5) group in the NMR spectrum of the latter. The location of the

secondary OH function at C(5) was supported by a COSY cross-peak of H–C(5) with H–C(6) and HMBCs with C(3), C(4), and C(7). The C(12) was assigned by the HMBCs H–C(9)/C(10) and CH_2(13)/C(12). A NOESY experiment (*Fig. 1*) was performed to ascertain the relative configuration at C(20), of Me(16) and Me(17), and at C(6), C(5), and C(9). The presence of mutual correlations between H–C(1) and Me(16), and H–C(1) and Me(17) suggested that they all are on the β-side of the molecule, and H–C(6) and H–C(5) are on the α-side. Taking all these spectroscopic data into account, the structure of cespihyptin W (**1**) was elucidated as (+)-(1β,5β,6β,7*E*,9β,20α)-5,6,20-trihydroxyverticilla-4(18),7,11-trien-10-one.

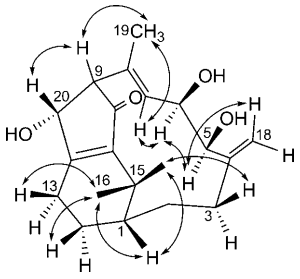


Fig. 1. *Key NOESY correlations and relative configuration of* **1**[1])

Cespihypotin X (**2**) was isolated as an optically active amorphous solid. 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–C(5) of **1** (δ(H) 4.35 (H–C(5)); δ(C) 78.7 (CH)) was replaced by a CH_2 moiety (δ(H) 2.00–2.04 and 2.57–2.63; δ(C) 44.7 (CH_2)), and the exocyclic CH_2(18)=C(4) of **1** (δ(H) 4.97 and 5.01; δ(C) 147.7 (C) and 112.2 (CH_2)) was converted to the primary-alcohol moiety CH_2(18)OH (δ(H) 3.80 and 4.41; δ(C) 60.3 (CH_2)), and the C=C bond was now situated between C(4) and C(3) (δ(H) 5.10; δ(C) 132.6 (CH) and 133.0 (C)). Both COSY cross-peaks H–C(6)/CH_2(5) and H–C(7) and the HMBCs from CH_2(5) to C(6), C(7), C(3), and C(18), as well as the HMBCs from CH_2(18) to C(5), C(3), and C(4) confirmed these assignments. NOESY Correlations (*Fig. 2*) indicated that Me(16), Me(17), H–C(7), and H–C(1) are on the β-side of the molecule, while H–C(6) is on the α-side. Thus, the structure of cespihypotin X (**2**) was established as (–)-(1β,3*Z*,6β,7*E*,9β,20α)-6,18,20-trihydroxyverticilla-3,7,11-trien-10-one.

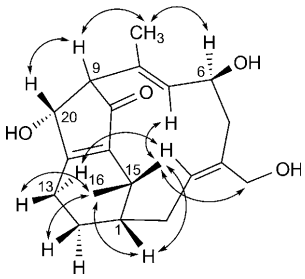


Fig. 2. *Key NOESY correlations and relative configuration of* **2**[1])

The ^{1}H- and ^{13}C-NMR spectra of the optically active cespihypotin Y (**3**) (*Tables 1* and *2*) revealed a high similarity to **2** possessing the same tricyclic ring system, but differing in the substituents. The allylic CH_2(18)OH group of **2** (δ(H) 3.80 and 4.41; δ(C) 60.3 (CH_2)) was changed to an α,β-unsaturated CHO moiety in **3** (δ(H) 10.12; δ(C) 194.1 (C)). The latter change of functionality brought about a change in the chemical shifts of the vicinal H- and C-atoms (**2** *vs.* **3**: δ(H) 5.10 *vs.* 6.39 (H–C(3)), and 2.00–2.04 and 2.57–2.63 *vs.* 1.90–1.94 and 2.93 (CH_2(5)); δ(C) 132.6 *vs.* 154.9 (C(3)), 133.0 *vs.* 136.9 (C(4)), and 44.7 *vs.* 39.4 (C(5))). Notable in the ^{1}H-NMR spectrum of **3** is the low-field chemical shift of H–C(3) (δ(H) 6.39) due to its β-position with respect to the CH=O group. The HMBCs H–C(18)/C(4), C(5), and C(3) clearly positioned the CH(18)=O group at C(4). The relative configuration of **3** was deduced from a NOESY experiment (*Fig. 3*), which indicated that Me(16), Me(17), H–C(7), and H–C(1) are on the β-side of the molecule, while H–C(6) is on the α-side. The NOESY correlation of the CHO group (H–C(18)) with Me(17) without significant correlation with H–C(3), established the (*Z*)-configuration of the C(3)=C(4) bond. Therefore, the detailed analyses of the 1D- and 2D-NMR spectra led us to propose the structure of cespihypotin Y (**3**) as (–)-(1β,3*Z*,6β,7*E*,9β,20α)-6,20-dihydroxy-10-oxoverticilla-3,7,11-trien-18-al.

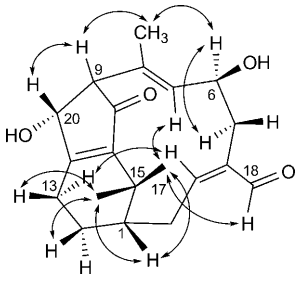


Fig. 3. *Key NOESY correlations and relative configuration of* **3**[1])

Analysis of 1D- and 2D-NMR data of the optically active cespihypotin Z (**4**) indicated that the segments C(1)–C(10) and C(15)–C(20) are similar to those of cespitularin F [6]. The H–C(13) resonating at δ(H) 4.81–4.86 (δ(C) 63.7) showed ^3J-HMBCs with the quaternary C(11) (δ(C) 148.4) of an α,β-unsaturated C=O group and the CH moiety resonating at δ(C) 45.3 (C(1)). The H–C(13) (δ(H) 4.81–4.86) showed COSY coupling to CH_2(14) (δ(H) 2.21–2.27), which in turn coupled to H–C(1) (δ(H) 1.86–1.92). The signal at δ(C) 165.8 was assigned to the quaternary C(12) based on its HMBCs with H–C(13) and H–C(9). The ^{13}C-NMR, COSY, and HMBC suggested that the location of the OH group is at C(13). The NOESY correlations H–C(1)/H–C(9) and Me(17), H–C(9)/H–C(20), and H–C(7)/Me(17) suggested that H–C(1), H–C(9), H–C(20), Me(16), and Me(17) are on the β-face of the molecule, and that H–C(6) and H–C(13) are α-oriented. The absence of correlation between H–C(7) and Me(19) was in agreement with an (*E*)-arrangement of the C(7)=C(8) bond. Based on the above findings, the structure of cespihypotin Z (**4**) was thus established as (+)-(1β,6β,7*E*,9β,13β,20α)-6,13,20-trihydroxyverticilla-4(18),7,11-trien-10-one.

The molecular formula of the optically active cespilactam A (**5**) was found to be $C_{17}H_{23}NO_2$ from the HR-ESI-MS and ^{1}H- and ^{13}C-NMR data (*Tables 1* and *2*), with 7 degrees of unsaturation. The IR absorption bands at 3383 and 1692 cm^{-1} were attributed to an OH group and an α,β-unsaturated γ-lactam moiety, respectively. All 17 C-atoms appeared in the ^{13}C-NMR spectrum of **5** (*Table 2*). The DEPT spectrum showed one aliphatic sp^3 Me (δ(C) 16.3 (Me(15)), one Me at a tetrasubstituted sp^2 C-atom (δ(C) 8.4 (Me(13)), six sp^3 CH_2 groups (δ(C) 39.4, 23.2, 36.2, 22.2, and 42.8, and one CH_2OH at δ(C) 61.9), one exocyclic CH_2=C group (δ(C) 107.2 (C(14))), one sp^3 CH (δ(C) 48.9 (C(5))), one trisubstituted sp^2 CH (δ(C) 119.7 (C(9))), and six quaternary C-atoms, including an amide C=O (δ(C) 38.0, 148.6, 140.1, 137.5, 124.2, and 172.4). On the basis of the above data, the remaining three degrees of unsaturation suggested that compound **5** contains a tricyclic eudesmanolide skeleton. Although the ^{13}C-NMR data for atractylenolactam [16] previously reported for this isolate from *Atractylodes macrocephala* was not published before, its ^{1}H-NMR spectrum was very close to that of **5**. The main difference between **5** and atractylenolactam [16] is that **5** contains a 2-hydroxyethyl group attached to the N-atom instead of the lactam H-atom which was resonating at δ(H) 7.36. COSY Cross-peaks from CH_2(17) to CH_2(16) and HMBCs from CH_2(16) to C(17), C(12), and C(8) suggested these assignments. The detailed NOESY correlation is illustrated in *Fig. 4*. A computer-modeled structure of **5** was generated by CS Chem 3D version 9.0 and a MM2 force-field calculation for the energy minimization as shown in *Fig. 5*. The result was consistent with the configuration of **5** as established by the NOESY experiments. The structure of cespilactam A was therefore determined as **5**.

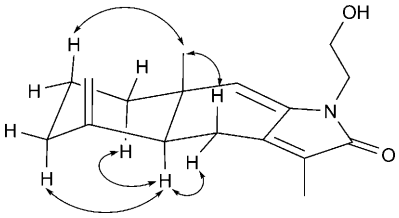


Fig. 4. *Key NOESY correlations and relative configuration of* **5**

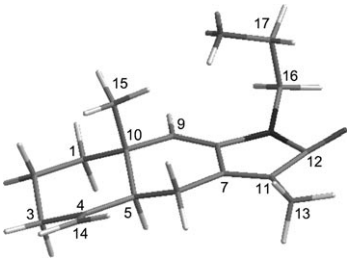


Fig. 5. *Computer-generated perspective model for* **5**[1]) (MM2 force field calculations)

The authors thank the *National Science Council*, R.O.C. (NSC-97-2113-M-002-016), for providing financial support. We appreciate Mrs. *C.-L. Ho*, *R.-R. Wu*, and *S.-C. Yu* of the *NSC* Southern NMR and MS Instrument Center for measuring high-resolution NMR (500 MHz) and MS data.

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*; SiO_2 *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}. ^{1}H- 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); δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. EI- 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 with the School of Pharmacy, College of Medicine, National Taiwan University, Taipei, Taiwan.

Extraction and Isolation. The soft coral *C. hypotentaculata* (dry; 1.1 kg) was extracted with CH_2Cl_2/EtOH 1:1 (3×10 l) at r.t., and the extract was concentrated under vacuum. The crude extract was partitioned between AcOEt and H_2O 1:1. The AcOEt-soluble portion (100 g) was subjected to FC (SiO_2, hexane/AcOEt $100:0 \rightarrow 0:100$, then AcOEt/MeOH $10:1 \rightarrow 3:1$): *Fractions 1–13*. *Fr. 9* (2.5 g) was separated by CC (*Sephadex LH-20*, CH_2Cl_2/MeOH 1:1) followed by reversed-phase HPLC (MeOH/MeCN/H_2O 4:1:5): **2** (8 mg), **3** (1 mg), and **4** (3.5 mg). *Fr. 10* (2 g) was subjected to CC (*Sephadex LH-20*, CH_2Cl_2/MeOH 1:1) followed by reversed-phase HPLC (MeOH/MeCN/H_2O 6:1:3): **1** (5 mg) and **5** (4.5 mg).

Cespihypotin W (= rel-*(1*R*,2*S*,5*R*,11*S*,12*R*,13*E*)-1,2,4,5,6,7-Hexahydro-1,11,12-trihydroxy-4,4,14-trimethyl-10-methylene-2,5-hept[1]eno-3*H*-inden-3-one*; **1**): Colorless amorphous solid. $[\alpha]_D^{25} = +76.1$ (c = 0.3, CH_2Cl_2). UV (MeOH): 234 (3.28). IR (neat): 3385, 1689. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 355.1883 ($[M+Na]^+$, $C_{20}H_{28}NaO_4^+$; calc. 355.1885).

Cespihypotin X (= rel-*(1*R*,2*S*,5*S*,9*Z*,12*S*,13*E*)-1,2,4,5,6,7-Hexahydro-1,12-dihydroxy-10-(hydroxymethyl)-4,4,14-trimethyl-2,5-hepta[1,5]dieno-3*H*-inden-3-one*; **2**): Colorless amorphous solid. $[\alpha]_D^{25} = -33.6$ ($c = 0.4$, CH_2Cl_2). UV (MeOH): 236 (3.27). IR (neat): 3376, 1692. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 355.1883 ($[M+Na]^+$, $C_{20}H_{28}NaO_4^+$; calc. 355.1885).

Cespihypotin Y (= rel-*(1*R*,2*S*,5*S*,9*Z*,12*S*,13*E*)-2,3,4,5,6,7-Hexahydro-1,12-dihydroxy-4,4,14-trimethyl-3-oxo-2,5-hepta[1,5]dieno-1*H*-indene-10-carboxaldehyde*; **3**): Colorless amorphous solid. $[\alpha]_D^{25} = -56.3$ ($c = 0.1$, CH_2Cl_2). UV (MeOH): 238 (3.65). IR (neat): 3394, 1697. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 353.1727 ($[M+Na]^+$, $C_{20}H_{26}NaO_4^+$; calc. 353.1729).

Cespihypotin Z (= rel-*(1*R*,2*S*,5*R*,7*R*,12*S*,13*E*)-1,2,4,5,6,7-Hexahydro-1,7,12-trihydroxy-4,4,14-trimethyl-10-methylene-2,5-hept[1]eno-3*H*-inden-3-one*; **4**): Colorless amorphous solid. $[\alpha]_D^{25} = +41.7$ (c = 0.4, CH_2Cl_2). UV (MeOH): 232 (3.26). IR (neat): 3416, 1695. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 355.1887 ($[M+Na]^+$, $C_{20}H_{26}NaO_4^+$; calc. 355.1885).

Cespilactam A (= rel-*(4a*R*,8a*R*)-1,4,4a,5,6,7,8,8a-Octahydro-1-(2-hydroxyethyl)-3,8a-dimethyl-5-methylene-2*H*-benz[f]indol-2-one*; **5**): Colorless amorphous solid. $[\alpha]_D^{25} = +35.2$ ($c = 0.2$, CH_2Cl_2). UV (MeOH): 240 (3.75). IR (neat): 3383, 1692. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 296.1628 ($[M+Na]^+$, $C_{17}H_{23}NNaO_2^+$; calc. 296.1626).

REFERENCES

[1] B. F. Bowden, J. C. Coll, J. M. Gulbis, M. F. Mackay, R. H. Willis, *Aust. J. Chem.* **1986**, *39*, 803.
[2] B. F. Bowden, J. Braekman, S. J. Mitchell, *Aust. J. Chem.* **1980**, *33*, 927.
[3] B. F. Bowden, J. C. Coll, S. J. Mitchell, G. J. Stokie, J. F. Blount, *Aust. J. Chem.* **1978**, *31*, 2039.
[4] K. P. Burns, R. Kazlauskas, P. T. Murphy, R. J. Wells, P. Schonholzer, *Aust. J. Chem.* **1982**, *35*, 85.
[5] C.-Y. Duh, C.-H. Li, S.-K. Wang, C.-F. Dai, *J. Nat. Prod.* **2006**, *69*, 1188.
[6] C.-Y. Duh, A. A. H. El-Gamal, S.-K. Wang, C.-F. Dai, *J. Nat. Prod.* **2002**, *65*, 1429.

[7] Y.-C. Shen, Y. B. Cheng, J. Kobayashi, T. Kubota, Y. Takahashi, Y. Mikami, J. Ito, Y.-S. Lin, *J. Nat. Prod.* **2007**, *70*, 1961.
[8] Y.-C. Shen, Y.-R. Wu, J.-J. Lin, K.-L. Lo, Y.-C. Kuo, A. T. Kalil, *Tetrahedron* **2007**, *63*, 10914.
[9] Y.-C. Shen, J.-J. Lin, Y.-R. Wu, J.-Y. Chang, C.-Y. Duh, K.-L. Lo, *Tetrahedron Lett.* **2006**, *47*, 6651.
[10] Y.-C. Shen, C.-J. Ho, Y.-H. Kuo, Y.-S. Lin, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2369.
[11] Y.-C. Shen, Y.-S. Lin, Y.-H. Kuo, Y.-B. Cheng, *Tetrahedron Lett.* **2005**, *46*, 7893.
[12] C. Zhang, J. Li, J. Su, Y. Liang, X. Yang, K. Zheng, L. Zeng, *J. Nat. Prod.* **2006**, *69*, 1476.
[13] B. Karlsson, A.-M. Pilotti, A.-C. Söderholm, T. Norin, S. Sundin, M. Sumimoto, *Tetrahedron* **1978**, *34*, 2349.
[14] F. Nagashima, A. Tamada, N. Fujii, Y. Asakawa, *Phytochemistry* **1997**, *46*, 1203.
[15] S. Basar, A. Koch, W. A. König, *Flavour Fragance J.* **2001**, *16*, 315.
[16] Z.-L. Chen, W.-Y. Cao, G.-X. Zhou, M. Wichtl, *Phytochemistry* **1997**, *45*, 765.

Received March 18, 2009