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New Terpenoids from a *Cacospongia* sp. from the Philippines

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Dedicated to Professor Paul J. Scheuer in recognition of his 50th year as a faculty member of the University of Hawaii

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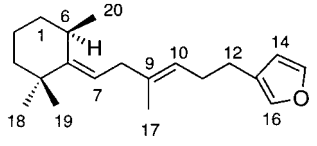
Abstract—Four new terpenoids, cacospongins A (**1**), B (**2**), C (**3**) and D (**4**), have been isolated from the Philippine sponge *Cacospongia* sp. Also isolated were 15,16-epoxy-8(17),13(16),14-labdatriene (**5**), ambliofuran (**6**) and luffariellolide (**7**). The structures of compounds **1**–**7** were determined by means of spectroscopic evidence.

Introduction

The marine sponge genus *Cacospongia* (order Dictyoceratida, family Thorectidae) is an important source of polycyclic sesterterpenoids, many of which have been reported to possess antitumoral and/or antipredatory activities. However, members of this genus collected from different locations appear to produce chemically distinct terpenoids. For example, Mediterranean *Cacospongia* species collected from the Bay of Naples and the Bay of Taranto provided mostly tetracarbocyclic scalarane type sesterterpenoids and related pyrroloterpenes.[1–3] Linear C_{21} difuran terpenoids have been reported from *C. scalaris* collected at Cap de Nice[4] while the same species collected from the northern Adriatic yielded 23,24-bishomoscalarenes.[5] A Caribbean sponge, *Cacospongia* cf. *linteiformis*, yielded a series of unprecedented bi-, tetra- and pentacyclic sesterterpenes,[6,7] while Australian collections have been reported to yield a number of brominated meroterpenoids.[8,9] Geographical variations in the chemistry of *Cacospongia* metabolites prompted us to study a specimen of *Cacospongia* collected from the Philippines. The hexane and $CHCl_3$ extracts of this specimen yielded seven compounds representing diterpene (**1**, **5**, **6**), mixed biogenesis (**2**, **3**, **4**) and sesterterpene (**7**) classes. The current study deals with the isolation, structure elucidation and taxonomic importance of compounds **1**–**7**.



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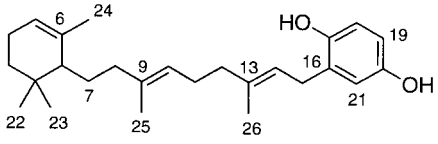

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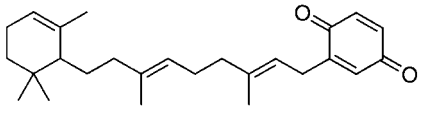

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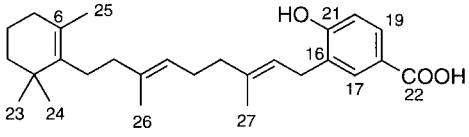

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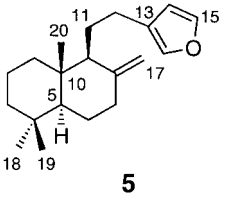

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Keywords: *Cacospongia*; cacospongins A, B, C, D; 15,16-epoxy-8(17),13(16),14-labdatriene; ambliofuran; luffariellolide.

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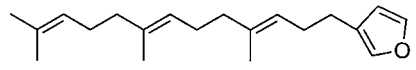
Table 1. ^{1}H NMR spectral data of cacospongins A–D (**1**–**4**), (500 MHz, $CDCl_3$) (Chemical shifts (δ) are in ppm. Coupling constants (J) in Hz are given in parentheses)

Position	1	2	3	4
1	1.42–1.56 m	5.24 (br t, 6.8)	5.26 br s	1.88 (t, 6.8)
2	1.83 (dt, 3.4/12.8) 1.95 m	1.92 m	1.94 m	1.53 m
3	1.32 (dt, 3.4/12.8) 1.45 m	1.88 m	1.89 m	1.39 m
5		1.38 m	1.40 m	
6	1.56 m			
7	5.38 br s	1.08 m	1.06 m	1.99 m
8	1.94 m	1.96 m	2.03 m	1.99 m
10	5.13 (t, 6.8)	5.07 m	5.07 (t, 6.8)	5.09 (br t, 6.8)
11	2.21 (q, 7.7)	2.06 m	2.08 m	2.10 m
12	2.47 (t, 7.7)	2.04 m	2.10 m	2.09 m
14	6.25 br s	5.29 (br t, 6.8)	5.14 (t, 6.8)	5.33 br s
15	7.32 br s	3.28 (d, 6.8)	3.12 (d, 7.7)	3.38 (d, 7.7)
16	7.19 br s			
17	1.56 s			7.87 br s
18	1.01 s	6.66 (d, 8.5)	6.74 (br d, 10.3)	
19	1.60 s	6.55 (dd, 8.5/3.4)	6.68 (dd, 10.3/2.6)	7.84 (dd, 8.5/2.5)
20	0.93 (d, 6.8)			6.83 (d, 7.7)
21		6.58 (d, 3.4)	6.51 br s	
22		0.84 s	0.84 s	
23		0.89 s	0.90 s	0.97 s
24		1.65 s	1.65 s	0.97 s
25		1.57 s	1.58 s	1.56 s
26		1.72 s	1.61 s	1.62 s
27				1.78 s



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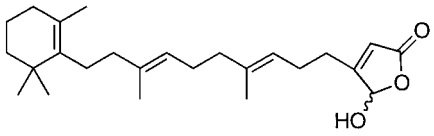

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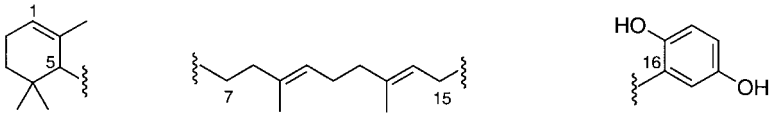
Results and Discussion

The organism *Cacospongia* sp. was extracted with MeOH and MeOH:$CHCl_3$ (9:1) mixtures. The combined extracts were filtered, dried, and subjected to a solvent partitioning scheme.[10] Purification of the hexane extract was carried out by a combination of flash chromatography (FC), preparative thin layer chromatography (PTLC) and C-18 HPLC to afford compounds **1**, **2**, **5** and **6**. Separation of the $CHCl_3$-soluble material by silica FC and C-18 HPLC led to the isolation of compounds **2**, **3**, **4** and **7**.

Compound **1** was obtained as a colorless oil. HREIMS data of **1** was in accordance with the molecular formula $C_{20}H_{30}O$ (*m/z* 286.2315 $[M]^+$). The ^{13}C NMR spectrum of **1** (Table 2) revealed twenty carbons eight of which were sp^2 hybridized (δ 111.1, d; 122.6, d; 123.1, d; 125.0, s; 137.1, s; 139.5, s; 138.8, d; 142.5, d) indicating the presence of six degrees of unsaturation. The ^{1}H NMR spectrum of **1** (Table 1) contained signals characteristic of a β-substituted furan (δ 6.25, br s; 7.19, br s; 7.32, br s) and two exocyclic double bonds (δ 5.13, t, J=6.8 Hz; 5.38, br s), plus one secondary and three tertiary methyl groups (δ 0.93, d, J=6.8 Hz; 1.01, s; 1.56, s; 1.60, s). NMR data coupled with the MS data suggested that **1** contained an additional carbocyclic ring. An HMQC experiment established the one-bond proton–carbon connectivities and a gradient HMBC experiment provided long range proton and carbon correlations. Detailed inspection of the ^{1}H NMR and DQF-COSY spectra of **1** indicated the presence of three spin systems. The

Table 2. ^{13}C NMR spectral data of compounds **1**–**5** (δ in ppm, 125 MHz, $CDCl_3$)

Carbon	1	2	3	4	5
1	27.4 t	119.8 d	119.8 d	32.8 t	39.0 t
2	35.6 t	23.1 t	23.1 t	19.6 t	24.1 t
3	34.6 t	32.6 t	32.5 t	39.9 t	42.1 t
4	39.5 s	32.7 s	32.8 s	35.0 s	33.6 s
5	139.5 s	48.9 d	49.0 d	137.2 s	55.5 d
6	37.6 d	136.9 s	136.8 s	127.0 s	24.4 t
7	122.6 d	31.6 t	31.7 t	27.9 t	38.3 t
8	23.9 t	40.5 t	40.6 t	40.3 t	148.6 s
9	137.1 s	136.4 s	136.5 s	136.6 s	56.1 d
10	123.1 d	123.6 d	123.6 d	123.1 d	39.6 s
11	28.4 t	26.4 t	26.5 t	26.4 t	19.4 t
12	25.0 t	39.7 t	39.7 t	39.7 t	23.6 t
13	125.0 s	138.7 s	140.2 s	138.9 s	125.6 s
14	111.1 d	121.3 d	117.6 d	121.0 d	111.0 d
15	142.5 d	29.8 t	27.4 t	29.5 t	142.6 d
16	138.8 d	128.2 s	148.5 s	126.9 s	138.7 d
17	16.1 q	148.3 s	187.6 s	132.4 d	106.2 t
18	26.4 q	116.6 d	136.3 d	121.6 s	33.6 q
19	19.5 q	113.7 d	136.7 d	130.3 d	21.7 q
20	15.9 q	149.3 s	187.9 s	115.6 d	14.5 q
21		116.6 d	132.3 d	159.6 s	
22		27.5 q	27.6 q	171.4 s	
23		27.4 q	27.4 q	28.7 q	
24		23.5 q	23.5 q	28.7 q	
25		16.1 q	16.1 q	19.8 q	
26		16.2 q	16.2 q	16.1 q	
27				16.3 q	



a **b** **c**

Figure 1. Substructures developed for compound **2**.

secondary methyl group (H_3-20) coupled to a methine proton (H-6; δ 1.56, m) which in turn coupled to methylene signals assigned as H_2-1. Additional homonuclear couplings between H_2-1, H_2-2 and H_2-3 completed the first spin system. The second spin system could be traced from the coupling of the olefinic proton (H-7, δ 5.38) to H_2-8 (δ 1.94 m) and H-6. The latter coupling also established that H-6 was in an allylic position relative to the double bond between C-5 (δ 139.5) and C-7 (δ 122.6). Further proof for this assumption was provided by correlations observed in the HMBC spectrum (H-1/C-5, H-1/C-6, H-7/C-5, H-7/C-8, H_3-20/C-1 and H_3-20/C-6). Similar cross peaks from both H_3-18 and H_3-19 to C-3 (δ 34.6), C-4 (δ 39.5), C-5, C-6 (δ 37.6) and C-7 ascertained the structure of **1** from C-1 through C-8. $\Delta^{5,7}$ was assigned *E* geometry based on an NOE observed between H-7 and H_3-19 (δ 1.60). The last proton network was assigned on the basis of COSY couplings from an sp^2 proton resonating at δ 5.13 (H-10) to H_2-11 (δ 2.21, q, J=7.7 Hz), and from H_2-11 to H_2-12 (δ 2.47, t, J=7.7 Hz). HMBC correlations between the latter protons and the furan carbons (C-13 to C-16) clearly showed the attachment of the furan at C-12. Additional $^1H-^{13}C$ long range correlations from H-8 to C-9 (δ 137.1) and C-10 (δ 123.1), as well as from H_3-17 (δ 1.56) to C-8 (δ 23.9) and C-9 justified the position of the vinylic methyl function (CH_3-17) and thus, the linkage of the isoprene chain at C-7/C-12. Configuration of $\Delta^{9,10}$ was also assigned to be *E* on the basis of the chemical shift of the latter methyl group (δ 16.1). These data generated the planar structure of **1**. Relative stereochemistry of the unique chiral center at C-6 was established by a combination of HYPERCHEM molecular modeling[11] and 2D NOESY studies. Compound **1** was modeled using both molecular mechanics geometry optimization (MM+) and PM3 semi-empirical geometry optimization. Steepest Descent and Polak–Ribiere methods were chosen to drive minimization. An NOE correlation was observed between H_3-18 (δ 1.01) and H-6 (δ 1.56) indicating their diaxial relationship. HYPERCHEM also showed H_3-18 and H-6 to be 2.77 Å apart, appropriate for a prominent nuclear Overhauser coupling. When the conformation of H_3-18 was changed to equatorial, these protons were 4.28 Å apart. Molecular modeling also indicated that the olefinic proton H-7 was too far from H_3-20 (4.2 Å) or H-6 (4.12 Å) to show any dipolar coupling. However, H-7 had a strong NOE correlation with H_3-19 with an interatomic distance of 2.42 Å. All this evidence implied that H-6 was axial and α-oriented. We propose the trivial name of cacospongin A for compound **1**.

Cacospongin B (**2**) was assigned the molecular formula $C_{26}H_{38}O_2$ (*m/z* 382.2871, Δ=0.1 mmu) by HREIMS. The IR spectrum contained absorption bands at ν_{max} 3348 (OH), 1652 and 1606 (C=C) cm^{-1}. The UV spectrum showed absorptions typical of an aromatic moiety (λ_{max} 217, 290 nm). Indeed, examination of the ^1H NMR spectrum of **2** (Table 1) revealed the presence of a trisubstituted aromatic ring (δ 6.66, d, H-18; δ 6.55, dd, H-19; δ 6.58, d, H-21) and three trisubstituted double bonds (δ 5.24, t, H-1; δ 5.07, m, H-10; δ 5.29, t, H-14), accounting for seven of the eight degrees of unsaturation. Therefore, **2** had an additional ring. From these data combined with results of HMQC, HMBC and DQF-COSY experiments, it was possible to develop three substructures (**a**–**c**, Fig. 1) for **2**. The *Z* geometry of the double bond at C-1/C-6 and the *E* geometry of $\Delta^{9,10}$ and $\Delta^{13,14}$ in substructures **a** and **b** were deduced from the chemical shifts of the vinyl methyl resonances (δ 23.5, C-24; δ 16.1, C-25; δ 16.2, C-26). Substructures **a** and **b** were connected on the basis of $^1H-^1H$ homonuclear couplings between H-5 (δ 1.38) and H_2-7 (δ 1.08), plus $^1H-^{13}C$ long range couplings from H-7 to δ 48.9 (C-5), δ 119.8 (C-1) and δ 23.5 (C-24). The attachment of substructure **b** to **c** at C-15 was established by HMBC correlations from δ 128.2 (C-16), δ 148.3 (C-17) and δ 116.6 (C-21) to δ 3.28 (H_2-15). Comparison of the planar structure (**2**) with jaspaquinol[12] showed these two compounds to be positional isomers $\Delta^{1,6}$ in **2**, and $\Delta^{5,6}$ in jaspaquinol. The relative stereochemistry at C-5 could not be established by NOESY or molecular modeling studies as the spatial distance between H-5 and H_3-22/H_3-23 is nearly identical (Å 2.67 and 2.82, respectively) and the double bond at C-1 deforms the conformation of the monocarbocyclic ring.

Cacospongin C (**3**) was isolated as a vivid yellow oil with a molecular weight of *m/z* 380.2703 (HREIMS, $C_{26}H_{36}O_2$, Δ=0.0012 amu), two mass units less than **2**. The ^1H spectrum of **3** was basically the same as that of **2**, except for slight differences in the aromatic region (Table 1). Close examination of the ^{13}C signals in this region (δ 187.6, 187.9, 132.3, 136.3, 136.7 and 148.5) indicated the presence of a terminal *para*-monosubstituted benzoquinone function in **3** instead of the *p*-hydroquinone found in **2**. This assumption was further supported by a gradient HMBC experiment which contained couplings from H_2-15 (δ 3.12) to C-16 (δ 148.5), C-17 (δ 187.6), C-20 (δ 187.9) and C-21 (δ 132.3); from H-18 (δ 6.74) to C-16, C-17 and C-20; and from H-19 (δ 6.68) to C-21. H-18 and H-19 could easily be assigned on the basis of homonuclear coupling (J=10.3 Hz) observed in the DQF-COSY spectrum, although they did not show any HMBC correlation to one another. It is possible that cacospongin C (**3**) was an artifact resulting from oxidation of cacospongin B (**2**) during the isolation procedure.

The structure elucidation of cacospongin D (**4**) progressed rapidly once the molecular formula of $C_{27}H_{38}O_3$ was established from the HREIMS (*m/z* 410.2812 $[M]^+$, Δ= 0.9 mmu), which required nine degrees of unsaturation. ^1H

and ^{13}C NMR data of **4** (Tables 1 and 2) were also very similar to those of **2**. The major differences being the presence of a tetrasubstituted double bond (δ 127.0 s, 137.2 s) and a carboxylic acid group (δ 171.4 s) in **4**. The position of the first functionality at $\Delta^{5,6}$ was substantiated by cross peaks observed in the HMBC spectrum of **4** between H-1/C-5, H-1/C-6, H-1/C-25, H_3-25/C-5 and H-7/C-5. Correlations were also observed from δ 7.87 (H-17), δ 7.84 (H-19), and δ 6.83 (H-20) to the *C*OOH signal at δ 171.4 which led to the placement of the carboxylic acid functionality at C-18. Based on the chemical shift values observed in the ^{13}C NMR spectrum of **4**, configuration of the olefinic bond in the monocyclic ring as well as in the linear part of the molecule was determined to be the same as in compound **2**.

Compound **5** gave a molecular ion peak in the HREI-mass spectrum at *m/z* 286.2288 ($[M]^+$), corresponding to the same molecular formula ($C_{20}H_{30}O$) as **1**. The ^{13}C NMR of **5** (Table 2) displayed six sp^2 carbons which were attributed to a monosubstituted furan ring and an exocyclic double bond. This required **5** to have two carbocyclic rings. The ^1H NMR spectrum of **5** was very similar to that of **1** except that it contained one pair of coupled olefinic resonances (δ 4.54, d, J=1.7 Hz; δ 4.84, d, J=1.7 Hz) and only three tertiary methyl singlets (δ 0.67, 0.78, 0.84). These data indicated that one of the methyl groups in **5** was converted to an exocyclic double bond. All other structural assignments substantiated by 2D NMR experiments allowed the planar structure of **5** to be established as 15,16-epoxy-8(17),13(16),14-labdatriene. The relative stereochemical assignments within **5** were established by 1D and 2D NOESY experiments. These analyses showed the axial methyl group H_3-18, H-5, and H-9 to be on the same side of the molecule (α), while the equatorial H_3-19, as well as H_2-11, and H_3-20 to be on the β side. Therefore, **5** was a *normal* labdane diterpene. A computer-based literature survey showed **5** with antipodal stereochemistry had already been reported from a terrestrial plant, *Blepharispermum zanguebaricum*.[13] However, the absence of ^{13}C NMR and particularly the optical rotation data for the antipodal compound does not allow us to make a firm conclusion as to whether **5** is a new compound.

Compound **6** was identified as a linear furanoditerpene with the same molecular formula ($C_{20}H_{30}O$) as **1** and **5**. On the basis of the 1D and 2D NMR data, the structure of **6** was determined as ambliofuran, which was reported from the marine sponge *Dysidea amblia* by Walker and Faulkner.[14]

Compound **7** was obtained as a minor component of the $CHCl_3$ extract of *Cacospongia* sp. LREI- and LRFABMS indicated **7** to be a sesterterpene comprising a molecular formula of $C_{25}H_{38}O_3$ (*m/z* 386 $[M]^+$ and 387 $[M+H]^+$). 1D and 2D NMR data proved **7** to be a known sesterterpenoid, luffariellolide, which has previously been isolated from tropical marine sponges, *Luffariella* sp.[15] and *Fascaplysinopsis* sp.[16]

All compounds were tested against *Staphylococcus aureus* and methicillin-sensitive *S. aureus*. Two compounds, **2** and **4**, showed 12 mm zones of inhibition against both strains at 5 mg/ml in agar-diffusion assays. All other compounds were inactive at this concentration. MIC_{50} values were not determined.

Conclusion

Dictyoceratid sponges are well known for producing terpenoids, especially sesqui- and sesterterpenes.[17] Our findings are in accordance with the current taxonomic classification scheme, and support the inclusion of the family Dysideidae within the order Dictyoceratida[18] (rather than Dendroceratida) as ambliofuran occurs in both *Dysidea amblia* (Dysideidae) and the *Cacospongia* studied here. Additionally, luffariellolide had its distribution expanded to a third genus within the Thorectidae, viz. *Cacospongia*, *Fascaplysinopsis* and *Luffariella*, thus pointing to some homogeneity within the family. There is considerable variation in the terpenoid content of members of the genus *Cacospongia* with collection site. Sesterterpenoids, linear C_{21} difuran terpenoids, and brominated meroterpenoids have been previously isolated from this genus. From a Philippine *Cacospongia* sp., we now report furanolabdane and linear furanoditerpenes as well as diterpene-benzenoids which have never been detected in this genus before. The co-occurence of these compounds along with a sesterterpenoid in the same animal is also interesting. This is the first report of 15,16-epoxy-8(17),13(16),14-labdatriene (**5**) from a marine source. Cacospongin A (**1**) also deserves special attention. Although similar furanosesquiterpenes with the C-5/C-6 exocylic double bond have been reported from a marine sponge,[19] insertion of an additional isoprene unit to yield a diterpene is unknown. Jaspaquinol, a *Jaspis* sponge metabolite,[12] was the first example of a monocyclic diterpenoid-benzenoid isolated from nature. This study represents the second report of such mixed biogenesis products (cacospongins B–D, **2**–**4**) from a marine source.

Experimental

General procedures

Optical rotations were measured on a Jasco DIP-370 Digital Polarimeter. UV spectra were recorded in MeOH on a Hewlett–Packard 8452A diode array spectrophotometer. IR spectra were recorded using a Jasco FTIR-420 spectrophotometer. NMR spectra were obtained on a Varian instrument, operating at 500 MHz for ^1H and 125 MHz for ^{13}C NMR spectra. All NMR spectra were recorded at 26°C using the residual signal of nondeuterated solvents as internal reference. Mass spectra were taken on a Finnigan MAT 95 mass spectrometer. SiO_2 used for FC was Merck Kieselgel 60, particle size 0.040–0.063 mm (Merck 230–400 mesh ASTM). Whatman PK6F Silica 60 Å precoated glass plates (layer thickness 1000 μm) were used for PTLC. C-18 (J.T. Baker, 40 μm, 275 Å) was utilized for RP-FC. HPLC was performed using a Beckman 168 diode array HPLC system. Molecular modeling studies were performed using HYPERCHEM (Release 4) program.

Animal material

The *Cacospongia* sponge (sample no. PD96-1-27, small

voucher deposited at Departamento de Invertebrados, Museu Nacional, Universidade Federal do Rio de Janeiro 20940-040, Rio de Janeiro, Brazil) was collected in the Davao Gulf, Philippines, in November 1996. It was massive with a grey conulose surface and the cream colored interior was densely collagenous with large fibers; the entire sponge turned purplish brown in spirit. Apart from some clear misidentifications of dubious status, there were six species descriptions to be compared with the Philippine material studied here, none of which seem conspecific. *Cacospongia herdmani* Dendy is a thinly encrusting species from Ceylon and the Arabian Sea. *C. lamellosa* Esper is a thin dark-red plate from Madagascar, Australia, and Japan. *C. mycofijiensis* is known to have variable morphology (massive, lobate, tubular, stalked), a microconulose surface, and dark-brown/black live-color. It is widely distributed in the South and Indo Pacific. The darker color and less conspicuous conules seem to set both species apart. Finding latrunculin-A and/or dendrolasin in the Philippine specimen might have suggested their conspecificity, but this has not been verified. *C. ridleyi* Burton has very similar anatomy but a semi-repent habit with cylindrical lobes and attached foreign bodies. *Cacospongia* sp. from the Mergui Archipelago (Indian Ocean) had a yellowish fawn-color and encrusting habit. *C. symbiotica* Burton from the southern Arabian coast is pale brown to brownish-purple with a much more delicate anatomy; its name stems from associated bivalves which could be diagnostic for the species. We prefer to keep the Philippine sponge at generic rank, until a more comprehensive revision of species, particularly from the Indo-Pacific, assigned to *Cacospongia* is conducted.

Extraction and isolation

Frozen sponge material was exhaustively extracted with MeOH and MeOH–$CHCl_3$ (9:1) mixtures. The combined extracts were dried and partitioned between 10% H_2O in MeOH (100 mL) and hexane (3×100 mL). The concentration of the aqueous MeOH was adjusted to 30% by the addition of water (40 mL) before extraction with $CHCl_3$. All three phases were concentrated in vacuo and inspected by TLC and ^{1}H NMR. An aliqout (160 mg) of the hexane extract was fractionated over SiO_2 (FC) using hexane–EtOAc gradients to afford 25 main fractions. Of these, fr. 3 (**5**, 4 mg) and fr. 7 (**6**, 1 mg) were pure compounds. Fr. 2 was further separated by silica PTLC (hexane–EtOAc, 96:4) followed by C-18 HPLC using MeOH–H_2O (98:2) to yield **1** (1.4 mg). The last fraction of interest, fr. 16 was subjected to C-18 FC. Elution with 85% MeOH in H_2O gave compound **2** (8 mg). The $CHCl_3$-soluble material (600 mg) was also applied to silica FC using hexane–EtOAc gradients. This yielded three pure compounds, **3** (2.8 mg), **2** (120 mg), **4** (20 mg) and impure **7**. Final purification of **7** (2 mg) was achieved by C-18 HPLC using MeOH–H_2O (98:2) mixture as eluent.

Cacospongin A (1). Colorless oil, $[\alpha]_D=-14°$ (*c* 0.16, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 209 (3.9) nm; IR (film) ν_{max} 2934, 1664, 1644, 1501, 873 cm^{-1}; EIMS *m/z* 286 $[M]^+$ (1), 271 (<1), 243 (1), 204 (1), 189 (1), 123 (100), 109 (61), 81 (53); HREIMS 286.2315 (calcd for $C_{20}H_{30}O$, 286.2298); ^{1}H NMR (500 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (125 MHz, $CDCl_3$), see Table 2.

Cacospongin B (2). Colorless oil, $[\alpha]_D=-26°$ (*c* 0.63, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 217 (3.2) 290 (3.9) nm; IR (film) ν_{max} 3348, 2927, 1652, 1606 cm^{-1}; EIMS *m/z* 382 $[M]^+$ (47), 367 (3), 246 (30), 190 (12), 178 (30), 163 (35), 137 (73), 123 (100), 95 (40), 81 (67); HREIMS 382.2871 (calcd for $C_{26}H_{38}O_2$, 382.2872); ^{1}H NMR (500 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (125 MHz, $CDCl_3$), see Table 2.

Cacospongin C (3). Yellow oil, $[\alpha]_D=-85°$ (*c* 0.24, $CHCl_3$); IR (film) ν_{max} 2929, 1660 cm^{-1}; EIMS *m/z* 380 $[M]^+$ (6), 330 (9), 315 (24), 257 (6), 201 (14), 161 (100), 136 (54), 123 (49), 95 (37), 81 (82); HREIMS 380.2703 (calcd for $C_{26}H_{36}O_2$, 380.2715); ^{1}H NMR (500 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (125 MHz, $CDCl_3$), see Table 2.

Cacospongin D (4). Colorless oil, IR (film) ν_{max} 3300 (br), 2927, 1682, 1602, 1278 cm^{-1}; EIMS *m/z* 410 $[M]^+$ (3), 395 (1), 259 (5), 161 (9), 151 (28), 137 (100), 123 (21), 95 (40); HREIMS 410.2812 (calcd for $C_{27}H_{38}O_3$, 410.2821); ^{1}H NMR (500 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (125 MHz, $CDCl_3$), see Table 2.

15,16-epoxy-8(17),13(16),14-labdatriene (5). Colorless oil, $[\alpha]_D=-22°$ (*c* 0.14, $CHCl_3$); IR, ^{1}H NMR and LREIMS data are the same as reported;[13] HREIMS 286.2288 (calcd for $C_{20}H_{30}O$, 286.2298); ^{13}C NMR data as shown in Table 2.

Ambliofuran (6). Colorless oil; EIMS, ^{1}H and ^{13}C NMR data are identical to those reported.[14]

Luffariellolide (7). Colorless oil; EIMS, ^{1}H and ^{13}C NMR data are identical to those reported.[15,16]

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