Uniquely Modified Imidazole Alkaloids from a Calcareous *Leucetta* Sponge

Ru Angelie Edrada, Chad C. Stessman, and Phillip Crews*

Department of Chemistry and Biochemistry and Institute for Marine Sciences, University of California, Santa Cruz, California 95064

Received October 25, 2002

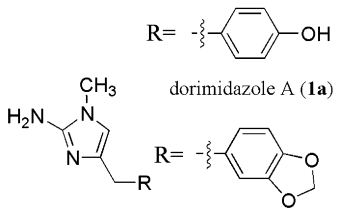
A Fijian collection of the calcareous sponge *Leucetta* sp. was investigated and yielded four new imidazole alkaloids. One compound, (+)-calcaridine A (**6**), is unique in its overall structure and consists of a geminally substituted 2-aminoimidazolidinone. An additional compound, (−)-spirocalcaridine A (**7**), is distinctive in its hexahydrocyclopentamidazol-2-ylidenamine spiro-linked to a cyclohexenone. A third compound, (−)-spirocalcaridine B (**8**), is the OCH_3 analogue of **7**. These compounds have unprecedented skeletons and functionality and are the first nonorganometalic chiral aminoimidazoles isolated from calcareous sponges. The two issues discussed here include the challenges associated with the structure elucidations of **6** and **7** and the relationships to previously encountered *Leucetta* metabolites.

Almost all of the natural products reported to date from marine sponges are based on studies of the class Demospongiae.[1] Alternatively, sponges of the other major class, Calcarea, can be found in all marine habitats, yet they have been subjects of limited previous chemical investigation. Two Calcarea genera, *Leucetta* and *Clathrina*, have received the widest attention. An early investigation resulted in the isolation of pteridine from low-light zones off Bermuda.[2] Overall, the literature of these two genera are rich with examples of achiral imidazole alkaloids that vary among five general structural frameworks. Lead compounds in each category are (a) dorimidazole A (**1a**) and preclathridine A (**1b**),[3] (b) naamine A (**2**),[4] (c) isonaamine A (**3**),[4] (d) leucettamine C (**4**),[5] and (e) 2-amino-2-deoxykealiiquinone (**5**).[6] The only chiral forms of these imidazole alkaloids are zinc complexes such as Zn^{2+}-(clathridine$^-$)$_2$, Zn^{2+}-(isonaamidine$^-$)$_2$, and (naamidine A$^-$)-Zn^{2+}-(naamidine G$^-$).[3b,7]

We recently began a comprehensive investigation of the chemistry and biology of calcareous sponges. Our repository contains specimens from both the Indo-Pacific and Caribbean. The most ubiquitious members of this group are organisms we refer to as "the lemon yellow" sponge. They are especially abundant in Indo-Pacific coral reefs and have spiculuous yellow lobes as shown by Colin.[8] The work described below was initiated on a Fijian organism also of lemon yellow color but having a globular potato shape with many apertures.[9] The chemistry of this specimen, reported below, differs greatly from previously observed Fijian specimens, possessing solitary lobes, of either spherical or globular shape.[3b]

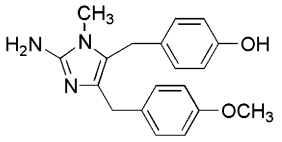
Results and Discussion

The *Leucetta* sp. (coll. no. 00111) was obtained from several sites south of Vitu Levu, Fiji. A methanol crude extract of this sponge provided an oil that was fractionated according to our standard scheme.[10] The 1:1 MeOH/H_2O solvent partition fraction (labeled as "FM") was pursued by reversed-phase HPLC and yielded three new compounds: (+)-calcaridine A (**6**), (−)-spirocalcaridine A (**7**), and (−)-spirocalcaridine C (**8**). On the basis of previous experience with the chemistry of *Leucetta*,[3−5] each of these compounds was assumed to be imidazole-containing, and

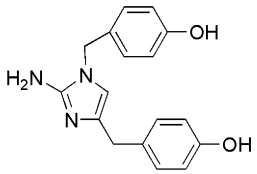


dorimidazole A (**1a**)

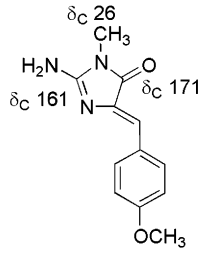
preclathridine A (**1b**)



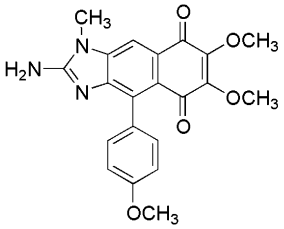
naamine A (**2**)



isonaamine A (**3**)



leucettamine C (**4**)



2-amino-2-deoxykealiiquinone (**5**)

* To whom correspondence should be addressed. Tel: 831 459 2603. Fax: 831 459 2935. E-mail: phil@chemistry.ucsc.edu.

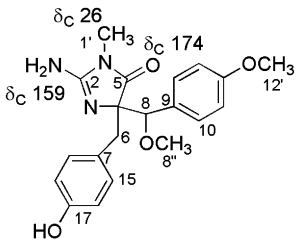
10.1021/np020503d CCC: $25.00
Published on Web 06/26/2003

Table 1. NMR Data (MeOH-d_4) at 500/125 MHz[a]

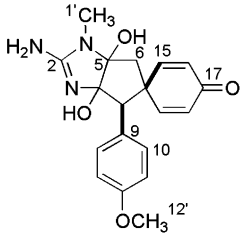
	6			**7**				**8**			
atom no.	$^{13}C(\delta_C)$	$^1H(\delta_H$, mult, J, Hz)	HMBC	$^{13}C(\delta_C)$	$^1H(\delta_H$, mult, J, Hz)	gHMBC	NOESY	$^{13}C(\delta_C)$	$^1H(\delta_H$, mult, J, Hz)	gHMBC	NOESY
2	158.6		1′	156.2		1′		156.2		1′	
4	73.1		6,8	94.8		6,8		97.3		6,8	
5	174.0		1′,6,8	96.6		6,1′		97.3		6,8,1′	
6	37.9	2.47d, 13.9 3.13d, 13.9	8,15	44.6	2.43d, 16.0 2.46d, 16.0		8,15,19,1′	45.2	2.43d, 16.0 2.47d, 16.0		1′
7	123.2		6,16,18	48.2		6,8,16,18		48.6		6,8	
8	84.2	4.55s	8′,10,14	62.6	3.70s	6,10,14	6,10,14,19	61.5	3.85s	6,10,14	
9	126.6		8,11,13	124.9		8,11,13		124.9		8,11,13	
10	129.2	7.35d, 8.7	8	131.0	7.21d, 8.5	8	8	131.0	7.19d, 8.5	8	
11	113.5	7.00d, 8.7		113.2	6.80d, 8.5			113.1	6.80d, 8.5		12′
12	160.5		10,11,12′, 13,14	159.9		10,14,12′		159.6		10,14,12′	
13	113.5	7.00d, 8.7		113.2	6.80d, 8.5			113.1	6.80d, 8.5		12′
14	129.2	7.35d, 8.7	8	131.0	7.21d, 8.5	8	8	131.0	7.19d, 8.5	8	
15	130.7	6.85d, 8.4	6	149.7	7.03dd, 9.8, 2.0	6,8	6,16	155.3	6.98d, 9.8	6,8	
16	114.7	6.61d, 8.4		129.7	6.28dd, 9.8, 2.0		15	129.8	6.28d, 9.8		
17	156.6		15,19	185.9		15,19		185.8		15,19	
18	114.7	6.61d, 8.4		129.1	6.12dd, 9.8, 2.0		19	129.1	6.12d, 9.8		
19	130.7	6.85d, 8.4	6	155.5	6.93dd, 9.8, 2.0	6	6,8,18	149.5	6.97d, 9.8	6,8,18	
1′	25.2	2.80s		24.9	3.01s		6	24.8	3.02s		6
4′								50.9	3.40s		
8′	55.9	3.82s									
12′	54.4	3.15s		54.2	3.73s			54.2	3.75s		11,13

[a] gHMBC correlations reported as ^1H to ^{13}C atom no., NOESY correlations reported as ^1H to ^1H atom no.

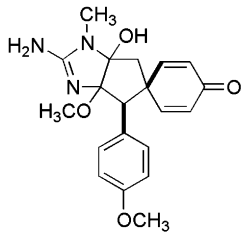
this supposition was quickly verified once the structural characterizations commenced.



(+) calcaridine A (**6**)



(-) spirocalcaridine A (**7**)



(-) spirocalcaridine B (**8**)

The first compound examined was (+)-calcaridine A (**6**), which gave an m/z = 370.1755 $[M + H]^+$ and required a $C_{20}H_{23}N_3O_4$ molecular formula. Its ^1H NMR spectrum along with the data of Table 1 revealed seven isolated spin systems consisting of four singlets (three of area 3 and one of area 1), one AB pattern characteristic of diastereotopic

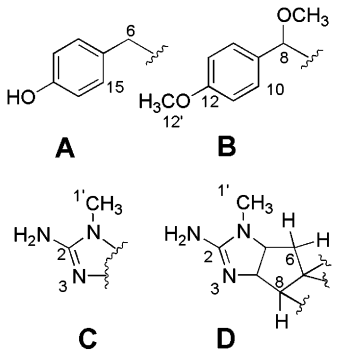
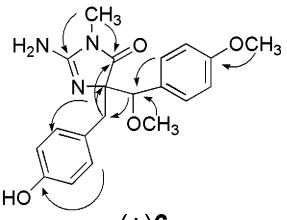


Figure 1. Substructures.

benzylic protons (H_2-6 δ 2.47, 3.13), and two simplified AA′XX′ multiplets characteristic of a *para*-disubstituted benzene ring. Among the three methyl singlets, two were OCH_3 groups (H_3-12′ δ_H 3.15 and H_3-8′ δ_H 3.82) and one was an *N*Me (H_3-1′ δ_H 2.80). The remaining singlet at δ_H 4.55 (H-8) was set as benzylic, and its carbon shift of δ_C 84.2 d indicated there was an oxygen attachment. Last, the resonances at δ_C 158.6 (C-2) and at $\delta_{C/H}$ 25.2/2.80 (Me-1′) were nearly identical to peaks observed in other *Leucetta*-derived imidazoles including **1**−**4**. On the basis of these data it was possible to draw the three substructures shown in Figure 1, including a *para*-hydroxybenzyl (**A**), a *para*-methoxy-α-methoxybenzyl (**B**), and a *N*-methylguanidyl (**C**). The assignment and interconnections of these fragments came from the selected gHMBC correlations shown in Figure 2 plus those outlined in Table 1. Confirmation of fragment **A** was verified from $^1H-^{13}C$ correlations from H-15 (δ_H 6.85) to C-17 (δ_C 156.6) and reciprocal correlations between benzylic CH_2-6 ($\delta_{C/H}$ 37.9/2.47, 3.13) and CH-15/19 ($\delta_{C/H}$ 130.7/6.85). Likewise fragment **B** was based on $^1H-^{13}C$ correlations from OMe-12′ (δ_H 3.15), H-11 (δ_H 7.00), and H-10 (δ_H 7.35) to C-12 (δ_C 160.5), from H-8 (δ_H 4.55) and H-11 (δ_H 7.00) to C-9 (δ_C 126.6), and reciprocal gHMBC correlations between OMe-8′ ($\delta_{C/H}$ 55.9/3.82) and CH-8 ($\delta_{C/H}$ 84.2/4.55). The final substructure **C** (of formula $C_2H_5N_2$) was reaffirmed by gHMBC correlations observed from *N*Me-1′(δ_H 2.80 s) to

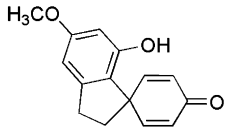


(+)**6**

Figure 2. Key gHMBC correlations.

δ_C 158.6 (C-2). The gHMBC peaks from H-8 to C-6 and from H_2-6 to both C-4 and C-5 justified connecting moieties **A** and **B** in a geminal fashion to C-4 and adding this piece to substructure **C**. At this juncture the only option to complete the structure involved creating the aminoimidazole ring by connecting N-3 and C-4 plus connecting C-4 and C-5. An additional key correlation was observed from *N*Me-1′ to amide carbonyl C-5, which allowed placing the Me-1′ at N-1 versus at N-3. Additional justification for the atom arrangement in the heterocyclic ring of calcaridine A (**6**) rested on its biogenetic relatedness to leucettamine C (**4**). Finally, as expected, the selected ^{13}C NMR shifts shown (see structures) for this pair were close in value.

Establishing the structure of (−)-spirocalcaridine A (**7**) was challenging due to an unusual arrangement of its oxygen functionality and the presence of seven quaternary carbons. The MS data established the molecular formula as $C_{19}H_{21}N_3O_4$, and comparison to the APT NMR formula of $C_{19}H_{17}$ indicated four heteroatom protons were present. Although the unsaturation number of 11 was the same as that of naamine A (**2**),[4] perhaps intimating their similar content of five- and six-membered rings, there were major differences in their comparative properties. The ^{1}H NMR (MeOH-d_4) data of **7** shown in Table 1 revealed six isolated spin systems consisting of three singlets (2 CH_3's and a CH), an AB pattern, a simplified AA′XX′ array, and a weakly coupled collection of four nonequivalent protons. The characteristic NMR shifts at the NCH_3 (δ_C 24.9, δ_H 3.01) and at C-2 in **7** accompanied by the gHMBC correlations from the NCH_3 to both C-2 (δ_C 156.2) and C-5 (δ_C 96.6) were consistent with the presence of substructure **C**, which could be extended to include the N-1/C-5 bond. A *para*-disubstituted benzene ring, identified by symmetrical multiplets at δ_H 6.80 and 7.21, was flanked by moieties including (a) an isolated benzylic proton H-8 (δ_H 3.70, s) and (b) a methoxy group (δ_H 3.73). These features were verified from the HMBC data shown in Table 1. Next, the coupled nonequivalent protons at δ_H 6.12, 6.28, 6.93, and 7.03 were eventually recognized as being part of a spiro-4,4-disubstituted cyclohexadienone ring system. Further support for this unique substructure came from comparison of our data to literature shifts. For example, the compound **7** C-17 (δ_C 185.9) carbonyl was close in value to that of 4,4-dimethylcyclohexadienone (δ_C 185.8),[11] and the shift of the compound **7** spiro carbon C-7 (δ_C 48.2, MeOH-d_4) was analogous to the δ_C 52.8 ($CDCl_3$) for the spiro carbon in sesquiterpenoid **9**.[12]



9

The remaining unsaturations and proton resonances of compound **7** were eventually assigned to bicyclic substructure **D**, shown in Figure 1. The interconnection of ring atoms 1, 2, 3, and 5 was established above. The protons attached to ring carbon atoms consisted of the isolated benzylic proton H-8 previously discussed and the diastereotopic aliphatic geminal protons at C-6 (δ_H 2.43, 2.46) displaying the characteristically large ^2J = 16 Hz. The three aliphatic carbons, C-6, C-7, and C-8, were joined together and fused into substructure **D** based upon gHMBC correlations from both H-8 (δ_H 3.70) and H_2-6 (δ_H 2.43, 2.46) to the bisallylic carbon C-7 (δ_C 48.2) and to α,α′-dienone moiety carbons C-15 (δ_C 149.7) and C-19 (δ_C 155.5). Additional gHMBC correlations from H_2-6 to aliphatic quaternary carbons C-4 (δ_C 94.8) and C-5 (δ_C 96.6) and from H-8 to C-4 meant that C-4 was also in the bicyclic ring **D**. Finally, the unusually low-field shifts of C-4 and C-5 indicated they were substituted with two electron-withdrawing groups consisting of an oxygen and nitrogen as required by constraints defined above. With C-7 defined previously as the terminus of the spiro-fused cyclohexadienone, this required C-8 as the location of the *p*-methoxyphenyl, further substantiated by the NOESY correlation between CH_3-1′ and H_2-6. The assignment of the diastereotopic protons (H-15/H-16 versus H-18/H-19) was based on the NOESY correlations observed between H-8 (δ_H 3.70) and H-19 (δ_H 6.93). Unfortunately, the NMR data did not allow assignment of the relative stereochemistry at the three chiral centers.

The structure elucidation of (−)-spirocalcaridine B (**8**) was based on analogies that could be made with **7**. The HRESI-TOF-MS *m/z* at 369.1760 $[M + H]^+$ established its molecular formula as $C_{20}H_{23}N_3O_4$, which was identical to that of **6** and greater than **7** by a CH-2. Comparison of the ^{1}H NMR data between **8** and **7** revealed identical spin systems except that of a new OCH_3 (δ_C 50.9, 3.40) consistent with their difference of one CH_2 group. Provisional assignment of an OCH_3 at C-4 was based on gHMBC and NOE data. Unfortunately, the only HMBC correlations observed from H_3-4′ (δ 3.40 s) were to the overlapping peaks at C-4 and C-5 (δ_C 97.3, 97.3). None of a series of NOE irradiations (by g1D difference) of H-8 (δ_H 3.85), H_2-6 (δ_H 2.43, 2.47), H-10 (δ_H 7.19), H-14 (δ_H 7.19), H-15 (δ_H 6.98), H-19 (δ_H 6.97), or H_3-1′ (δ_H 3.02) showed excitation of the resonance at δ_H 3.40. Similarly, NOE irradiation of the latter did not give signal enhancement for any other resonance. Between the two possible $-OCH_3$ substitution regioisomers, the one that is most consistent with the NOE data from the $-OCH_3$ is the structure having it attached at C-4. There are additional properties of spirocalcaridines A (**7**) and B (**8**) that deserve mention. Both compounds were observed by HPLC in approximately equal amounts in the crude extract. Compound **7** was stable for long periods of time when stored in methanol and was not transformed to compound **8** when warmed to 40 °C in this solvent. Likewise, compound **8** is extremely stable in methanol.

Conclusions

The chiral aminoimidazoles isolated here, (+)-calcaridine A (**6**) and (−)-spirocalcaridine A (**7**), contain several rare structural units that, taken together, are without precedent in the chemistry of calcareous sponges. These are the first examples of inherently chiral aminoimidazole-containing alkaloids encountered from *Leucetta*, as all previous optically active compounds derive chirality from the complexation with Zn^{2+}. The polycyclic nature of **7** is striking even though spiro-linked carbobicyclic systems are a common feature of plant- and marine algal-derived sesquiterpenes.[13] Such structures are less frequently encountered from

marine invertebrates.[14] Further, a cyclohexadienone ring spiro-linked to a five-membered carbocyclic ring does not appear to have been directly observed from marine natural products; however, the ring contraction of 17β-hydroxy-17α-methylandrosta-1,4-dien-3-one to yield a spiro-linked derivative via incubation with the green alga T76 *Scenedesmus quadricauda* has been reported.[15] There are obvious biosynthetic relationships that relate known achiral calcareous sponge metabolites to (−)-**6** and (−)-**7**, but unexplained is the process responsible for the chirality. Naamine A (**2**) provides a likely starting point for an intramolecular rearrangement to explain the connectivities in (−)-**6**. Similarly, distinct intramolecular cyclizations from **2** rationalize the 2D frameworks of **5** and (−)-**7**, respectively.

Experimental Section

General Experimental Procedures. NMR spectra were collected at 500 MHz for ^{1}H and 125 MHz for ^{13}C. Multiplicities of ^{13}C NMR peaks were determined using DEPT and gHMQC data. High-resolution mass measurements were obtained on a benchtop ESI-TOF apparatus. Other procedures were as previously published.[16]

Biological Material, Collection, and Identification. The *Leucetta* sp. (coll. no. 00111, 6.2 kg) was collected using scuba from a variety of habitats off the coast of Fiji, (S 18°19.19′, E 178°01.99′) and (S 18°19.36′, E 178°01.346′) at various depths. This sponge was identified by Dr. M. C. Diaz (UCSC, IMS) in reference to properties described in the literature.[17] Voucher specimens and underwater photos are available (from P.C.).

Extraction and Isolation. The sponge was preserved in the field according to our standard procedures and transported back to the laboratory at ambient temperature.[16] The collection was extracted with MeOH (3×), after which the solvent was removed and the resulting oil was partitioned between hexanes and 10% aqueous MeOH. The MeOH layer was adjusted to 50% aqueous MeOH and extracted with CH_2Cl_2. The MeOH/water layer was evaporated and yielded a yellow-brown oil (0.427 g). This was subjected directly to reversed-phase (C_{18}) HPLC (gradient 10% to 100% MeOH in 60 min), yielding minor components **6** (6.1 mg), **7** (5.4 mg), and **8** (6.3 mg).

(+)-Calcaridine A (6): yellow oil; $[\alpha]_D$ +1.6° (*c* 0.122, MeOH); ^{1}H NMR (MeOH-d_4, 500 MHz) and ^{13}C NMR (MeOH-d_4, 125 MHz), see Table 1 and Supporting Information Figure S1; ^{1}H−^{1}H COSY NMR correlations H-10−H-11, H-13−H-14, H-15−H-16, H-18−H-19; HRESIMS $[M + H]^+$ obsd 370.1755, calcd for $C_{20}H_{24}N_3O_4$ 370.1761.

(−)-Spirocalcaridine A (7): yellow oil; $[\alpha]_D$ −59.3° (*c* 0.108, MeOH); ^{1}H NMR (MeOH-d_4, 500 MHz) and ^{13}C NMR (MeOH-d_4, 125 MHz), see Table 1 and Supporting Information Figures S2 and S3; ^{1}H−^{1}H COSY NMR correlations H-10−H-11, H-13−H-14, H-15−H-16, H-18−H-19; HRESIMS $[M + H]^+$ obsd 356.1610, calcd for $C_{19}H_{22}N_3O_4$ 356.1605.

(−)-Spirocalcaridine B (8): yellow oil; $[\alpha]_D$ −50.8° (*c* 0.126, MeOH); ^{1}H NMR (MeOH-d_4, 500 MHz) and ^{13}C NMR (MeOH-d_4, 125 MHz), see Table 1 and Supporting Information Figures S4 and S5; ^{1}H−^{1}H COSY NMR correlations H-10−H-11, H-13−H-14, H-15−H-16, H-18−H-19; HRESIMS $[M + H]^+$ obsd 370.1760, calcd for $C_{20}H_{24}N_3O_4$ 370.1761. Attempts were made to obtain NMR data in different solvents, but limited solubility prevented the use of $CDCl_3$ or acetone-d_6, and extremely broad peaks were observed for DMSO-d_6.

Acknowledgment. Financial support was provided by grant NIH R01 CA 47135. M. C. Diaz (UCSC) generously provided sponge taxonomy analyses. Additional financial support at UCSC was provided by equipment grants from NSF BIR-94-19409 (NMR) and the Elsa U. Pardee Foundation (ESI-Quadrupole MS), and a supplement to NIH CA-52955 for the purchase of the ESI-TOF-MS. We thank M. L. Sanders for assistance in sponge collection. We appreciated the assistance from B. Aalbersberg, University of the South Pacific, Fiji, and A. Raiwalui, Permanent Secretary for the Director of Fisheries, Ministry of Agriculture, Fisheries, and Forests, Fishery Division, for obtaining administrative approvals to carry out research in Fiji.

Supporting Information Available: NMR spectra of **6**, **7**, and **8** (^{1}H, ^{13}C NMR) are available along with experimental ^{13}C NMR data for model compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Faulkner, D. J. *Nat. Prod. Rep.* **2001**, *18*, 1−49, and previous entries in this series.
(2) (a) Cardellina, J. H.; Meinwald, J. *J. Org. Chem.* **1981**, *46*, 4782−4784. (b) Pfleiderer, W. *Tetrahedron* **1988**, *44*, 3373−3378.
(3) (a) Alvi, K. A.; Crews, P.; Loughhead, D. G. *J. Nat. Prod.* **1991**, *54*, 1509−1515. (b) Alvi, K. A.; Peters, B. M.; Hunter, L. M.; Crews, P. *Tetrahedron* **1993**, *49*, 329−336.
(4) Carmely, K.; Kashman, Y. *Tetrahedron Lett.* **1987**, *28*, 3003−3006.
(5) (a) Carmely, S.; Ilan, M.; Kashman, Y. *Tetrahedron* **1989**, *45*, 2193−2200. (b) Crews, P.; Clark, D. P., Tenney, K. *J. Nat. Prod.* **2003**, *66*, 177−182.
(6) (a) Akee, R. K.; Carroll, T. R.; Yoshida, W. Y.; Scheuer, P. J.; Stout, T. J.; Clardy, J. *J. Org. Chem.* **1990**, *55*, 1944−1946. (b) Fu, X.; Barnes, J. R.; Do, T.; Schmitz, F. J. *J. Nat. Prod.* **1997**, *60*, 497−498.
(7) (a) He, H.; Faulkner, D. J. *J. Org. Chem.* **1992**, *57*, 2176−2178. (b) Mancini, I.; Guella, G.; Debitus, C.; Pietra, F. *Helv. Chim. Acta* **1995**, *78*, 1178−1184.
(8) See underwater photograph of specimen 230 p 60: Colin, P. L.; Arneson, C. *Tropical Invertebrates*; Coral Reef Press: Beverly Hills, 1995; p 60.
(9) For example see the underwater photographs of *Leucetta* sp. in: (a) Gosliner, T. M.; Behrens, D. W.; Williams, G. C. *Coral Reef Animals of the Indo-Pacific*; Sea Challengers: Monterey, 1996; entry no. 5, p 16. (b) Bertsch, H., Martin, K., Eds. *Animal Life from Africa to Hawai'i Exclusive of the Vertebrates*; Sea Challengers: Monterey 1996; p 16.
(10) Jaspars, M.; Rali, T.; Laney, M.; Schatzman, R. C.; Diaz, M. C. Schmitz, F. J.; Pordesimo, E. O.; Crews, P. *Tetrahedron* **1994**, *50*, 7367−7373.
(11) Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. In *Spectral Data for Structure Determination of Organic Compounds*, 2nd ed.; Freisenius, W., Huber, J. F. K., Pungor, E., Rechnitz, G. A., Simon, W., West, T. S., Eds.; Springer-Verlag: Berlin, 1989; p C190.
(12) Engstrom, K. *Phytochemistry* **1998**, *49*, 1585−1587.
(13) (a) Patriana, C.; Fenical, W.; Cocoran, E.; Clardy, J. *Tetrahedron Lett.* **1993**, *34*, 3371−3372. (b) Brennan, M. R.; Kim, I. K.; Erickson, K. L. *J. Nat. Prod.* **1993**, *56*, 76−84
(14) Barrow, C. J.; Blunt, J. W.; Munro, M. H. G. *Aust. J. Chem.* **1988**, *41*, 1755−1761
(15) DellGreca M.; Previtera, L.; Fiorentino, A.; Pinto, G.; Pollio, A. *Tetrahedron* **1996**, *52*, 13981−13990.
(16) Jaspars, M.; Rali, T.; Laney, M.; Schatzman, R. C.; Diaz, M. C.; Schmitz, F. J.; Pordesimo, E. O.; Crews, P. *Tetrahedron* **1994**, *50*, 7367−7373.
(17) See: "Spongeguide" available from Hooper, J.N.A.; www.qmuseum.qld.gov.au/organisation/sections/SessileMarineInvertebrates/index.asp.

NP020503D