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# Agelastatin E, Agelastatin F, and Benzosceptrin C from the Marine Sponge *Agelas dendromorpha*

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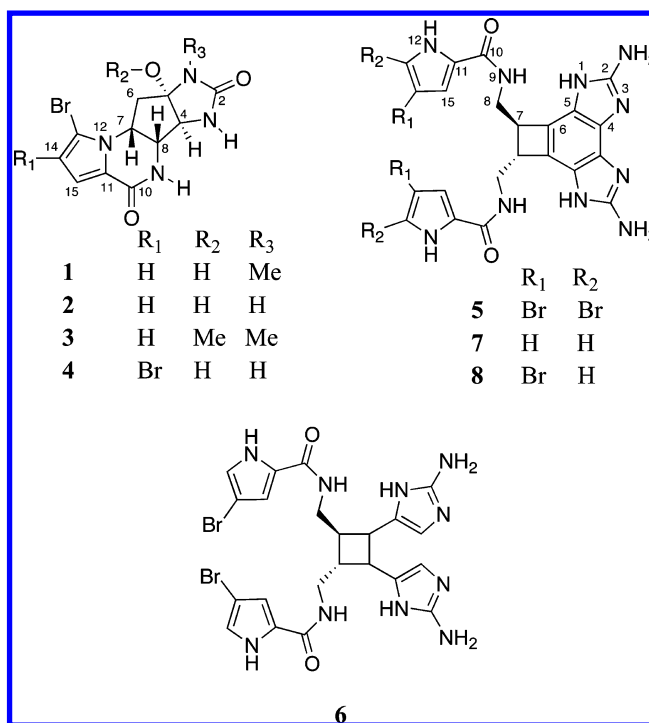
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The study of the *n*-butanol extract of the New Caledonian sponge *Agelas dendromorpha* led to the isolation and identification of three new pyrrole-2-aminoimidazole (P-2-AI) alkaloids, named agelastatins E (**3**) and F (**4**) and benzosceptrin C (**5**), together with 10 known metabolites, agelastatin A (**1**), agelastatin D (**2**), sceptrin (**6**), manzacidin A, tauroacidin A, taurodispacamide A, nortopsentin D, thymine, longamide, and 4,5-dibromopyrrole-2-carboxamide. Their structures were assigned by spectroscopic data interpretation. All the compounds were tested for cytotoxic activity.

Marine alkaloids possessing a pyrrole-2-imidazole (P-2-AI) structure are known to be some of the most common and structurally intriguing metabolites isolated from marine sponges. Over the last 30 years, a number of molecules have been encountered that likely arise from clathrocin, hymenidin, and oroidin precursors.<sup>3</sup> Many of these compounds are reported to have interesting biochemical activities, such as blocking  $\alpha$ -adrenoceptors,<sup>4</sup> serving as an antagonist of serotonergic receptors,<sup>5</sup> activating actomyosin ATPase,<sup>6</sup> and inhibiting kinase activity,<sup>7</sup> as well as antibacterial,<sup>8</sup> antifungal,<sup>8</sup> and antihistamine activities.<sup>9</sup> Among them, the immunosuppressive activity of palauamine,<sup>10</sup> the kinase inhibition of debromohymenialdesin,<sup>11</sup> the antitumor activity of giroline,<sup>12</sup> and the cytotoxicity of agelastatin A<sup>13</sup> are remarkable. Agelastatin A (**1**), along with a minute quantity of agelastatin B, was first reported from the sponge *Agelas dendromorpha*.<sup>13a</sup> Later on, in addition to agelastatins A and B, the closely related compounds agelastatins C and D were isolated from the sponge *Cymbastela* sp.<sup>13b</sup>

During our search for bioactive substances from marine organisms, we have previously reported several pyrrole-2-aminoimidazole (P-2-AI) alkaloids, together with a proposal for their biogenesis and biomimetic synthesis.<sup>14</sup> In line with the pursuit of biological activities and the structure-guided isolation for biosynthetic investigations, we have recently carried out a chemical study of the New Caledonian sponge *Agelas dendromorpha* (Lévi, 1993) (order Agelasida, family Agelasidae). The freeze-dried sponge was extracted with MeOH, and the extract was partitioned between *n*-BuOH and H<sub>2</sub>O. The *n*-BuOH fraction was subjected to silica gel column chromatography followed by preparative RP<sub>18</sub> HPLC to yield three new minor compounds, agelastatin E (**3**), agelastatin F (**4**), and benzosceptrin C (**5**) together with a series of known alkaloids. These were agelastatin A (**1**),<sup>13a</sup> agelastatin D (**2**),<sup>13b</sup> sceptrin (**6**),<sup>15</sup> manzacidin A,<sup>16</sup> tauroacidin A,<sup>17</sup> taurodispacamide A,<sup>18</sup> nortopsentin D,<sup>19</sup> thymine, longamide,<sup>20</sup> and 4,5-dibromopyrrole-2-carboxamide.<sup>21</sup> The structures of the known metabolites were determined by comparison of their <sup>1</sup>H and <sup>13</sup>C NMR spectra with those reported in the literature. Here, we describe the isolation of the new compounds **3**, **4**, and **5**.

The ESI mass spectrum of agelastatin E (**3**) showed pseudomolecular ion peaks at *m/z* 353:355 (1:1) [M + H]<sup>+</sup>, indicating the presence of one bromine atom in the molecule. The molecular formula of **3** was revealed as C<sub>13</sub>H<sub>15</sub><sup>79</sup>BrN<sub>4</sub>O<sub>3</sub> by HRESIMS. The



UV absorption at  $\lambda_{\text{max}}$  286 nm was attributed to a substituted pyrrole chromophore, while IR absorption at 3223, 1656, and 1642 cm<sup>-1</sup> indicated the occurrence of NH and amide carbonyl functionalities. The <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound **3** were similar to those of agelastatin A (**1**),<sup>13a</sup> except for an additional signal arising at  $\delta_{\text{H}}$  3.18 (s, 3H) for either an -OCH<sub>3</sub> or -NCH<sub>3</sub> group (Table 1). The position of the CH<sub>3</sub> with  $\delta_{\text{H}}$  3.18 ( $\delta_{\text{C}}$  50.8) was established as an -OCH<sub>3</sub> at C-5 on the basis of its HMBC correlation with  $\delta_{\text{C}}$  101.0 (C-5). The signal at  $\delta_{\text{H}}$  2.78 (3H, s) showed correlations with amide carbonyls at C-2 ( $\delta_{\text{C}}$  162.2) and 101.0 (C-5), confirming the presence of an NCH<sub>3</sub> group (Figure 1). The <sup>1</sup>H-<sup>1</sup>H COSY spectrum showed the connectivities from H-6a/b ( $\delta_{\text{H}}$  2.66, dd, *J* = 12.9, 6.6 Hz/2.14, dd, *J* = 12.9 Hz) to H-7 ( $\delta_{\text{H}}$  4.62, dd, *J* = 12.6, 6.6 Hz); H-7 to H-8 ( $\delta_{\text{H}}$  4.11, d, *J* = 5.4 Hz); and H-14 ( $\delta_{\text{H}}$  6.32, d, *J* = 4.1 Hz) to H-15 ( $\delta_{\text{H}}$  6.91, d, *J* = 4.1 Hz) for a cyclopentane ring and a monobromopyrrole moiety, respectively. The pyrrole signals at  $\delta_{\text{H}}$  6.32 (d, *J* = 4.1 Hz, H-14) and  $\delta_{\text{H}}$  6.91 (d, *J* = 4.1 Hz, H-15) showed HMBC correlations at  $\delta_{\text{C}}$  124.2 (C-11), 107.5 (C-13), 116.2 (C-15) and  $\delta_{\text{C}}$  124.2 (C-11), 107.4 (C-13), 114.0 (C-

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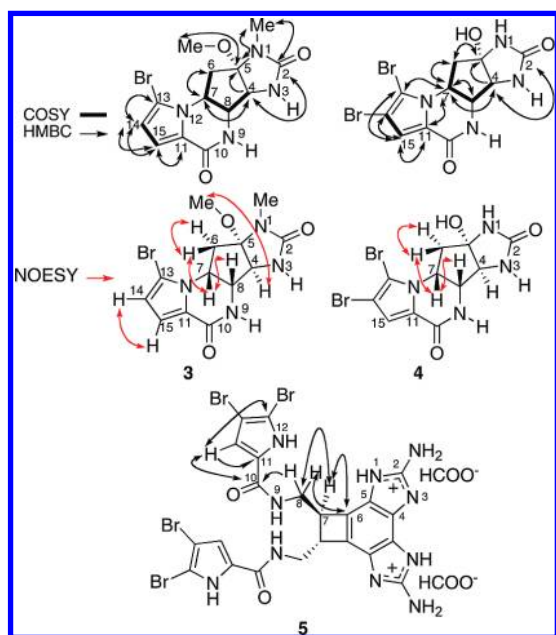
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**Table 1.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR Data for Agelastatins E (**3**) and F (**4**) Recorded in  $\text{CD}_3\text{OD}$  (600 MHz)

position	agelastatin E ( <b>3</b> )				agelastatin F ( <b>4</b> )			
	$\delta_{\text{C}}$	$\delta_{\text{H}}$ (J in Hz)	COSY	HMBC <sup>b</sup>	$\delta_{\text{C}}$	$\delta_{\text{H}}$ (J in Hz)	COSY	HMBC <sup>b</sup>
1-NH								
2	162.2				162.8			
3-NH		7.3				7.3		
4	61.2	4.08, bs		2, 5, 7, 8	69.5	3.92, bs		2, 5, 7
5	101.0				93.3			
6a	39.3	2.66, dd (12.9, 6.6)	H-6b, H-7	5, 6a, 7	43.7	2.58, dd (12.9, 6.6)	H-6b, H-7	4, 5, 6, 7, 8
6b		2.14, bt (12.9)	H-6a, H-7	5, 6a, 7, 8		2.24, bt (12.9)	H-6a, H-7	5, 6, 7
7	53.9	4.62, m (12.6, 6.6)	H-8	6, 11, 13	55.8	4.74, m (12.6, 6.6)	H-8	6, 7, 11, 13
8	62.2	4.11, d (5.4)	H-7	4, 6	62.2	4.14, d (5.5)	H-7	4, 5, 6
9-NH		7.92				8.1		
10	161.2				160.2			
11	124.2				125.0			
12								
13	107.4				108.7			
14	114.0	6.32, d (4.1)	H-15	11, 13, 15	101.1			
15	116.2	6.91, d (4.1)	H-14	11, 13, 14	117.1	6.98, s		11, 14
N-Me	24.7	2.78, s		2, 5, 6				
O-Me	50.8	3.18, s		5				

<sup>a</sup> Shifts of  $\text{D}_2\text{O}$  exchangeable protons were detected in  $\text{DMSO}-d_6$  at 500 MHz:  $\delta_{\text{H}}$  6.86, 6.39 for agelastatins E (**3**) and F (**4**);  $\delta_{\text{H}}$  5.7, 8.04, 8.34 for benzoscceprin C (**5**). <sup>b</sup> HMBC correlations are from the proton stated to the indicated carbon.

**Figure 1.** Key COSY, HMBC, and NOESY correlations of agelastatins E (**3**) and F (**4**) and benzoscceprin C (**5**).

14), respectively. The HMBC correlations of  $\delta_{\text{H}}$  4.62 (H-7) with  $\delta_{\text{C}}$  124.3 (C-11) and 107.4 (C-13) established the connection between the cyclopentane ring and the pyrrole moiety. Further analysis of the HMBC experiment established the connectivity of H-6 methylene protons at  $\delta_{\text{H}}$  2.66 (dd) and 2.14 (br t) to C-5, C-6, C-7 and C-5, C-6, C-7, C-8, respectively. The broad singlet at  $\delta_{\text{H}}$  4.08 (H-4) showed correlations with C-2, C-5, C-7, and C-8, while the doublet at  $\delta_{\text{H}}$  4.11 (H-8) showed correlations with C-4 and C-6. The quaternary carbon signals  $\delta_{\text{C}}$  162.2 (C-2), 101.0 (C-5), 124.3 (C-11), and 107.4 (C-13), invisible in the 1D  $^{13}\text{C}$  NMR spectrum, have been confirmed by HMBC experiment. Taken together, the data and the very similar 1D  $^1\text{H}$  NMR spectrum to that of agelastatin A (**1**) gave the structure **3** for this compound, which was named agelastatin E. NOESY experiments (Figure 1) showed correlations between the OMe group at position C-5 and H-4 on one hand and between H-7 and H-6/H-8 on the other hand, indicating the *cis*-fused cycles at C<sub>4</sub>–C<sub>5</sub> and C<sub>7</sub>–C<sub>8</sub>. The relative configuration for **3** was revealed to be the same as for agelastatin A (**1**). Whether agelastatin E (**3**) is a naturally methylated derivative of agelastatin A (**1**) or just a result of its dehydration and methoxylation is an

interesting question. The second process could occur during the purification process in the presence of MeOH.

Agelastatin F (**4**) was obtained as a white solid and was sparingly soluble in MeOH. The positive ESI-MS spectrum showed pseudomolecular ion peaks at  $m/z$  405, 407, and 409 (1:2:1) for the presence of two bromine atoms in the molecule. The molecular formula of **4** was revealed as  $\text{C}_{11}\text{H}_{10}\text{Br}_2\text{N}_4\text{O}_3$  by (–)-HRESIMS. The  $^1\text{H}$  NMR spectrum of **4** was very similar to that of agelastatin D (**2**),<sup>13b</sup> but lacked a proton signal at  $\delta_{\text{H}}$  6.33 (H-14), which is replaced by a Br atom, as revealed by the molecular formula. The pyrrole signal at  $\delta_{\text{H}}$  6.98 showed HMBC correlations to the carbons at  $\delta_{\text{C}}$  125.03 (C-11), 108.7 (C-13), and 101.1 (C-14) (Table 1). There were HMBC correlations from H-7 to the pyrrolic C-11 and C-13. The H-15 ( $\delta_{\text{H}}$  6.98) bonded to C-15 ( $\delta_{\text{C}}$  117.1) showed strong HMBC correlations with C-11 and C-14, allowing for only the 13,14 bromine substitution pattern, positioning the hydrogen at C-15. The strongly down-shifted C-14 ( $\delta_{\text{C}}$  101.1) and the comparison with NMR spectra published for agelastatin B<sup>13b,e</sup> indicated that this position was brominated. The UV absorption at  $\lambda_{\text{max}}$  288 nm was attributed to a substituted pyrrole chromophore. The IR spectrum showed absorption bands at 3254, 1681, and 1634  $\text{cm}^{-1}$  for OH, NH, and amide carbonyl groups. All of the connections were established by HMBC and COSY experiments. The  $^1\text{H}$ – $^1\text{H}$  COSY spectrum showed the connectivities from H-6a/b to H-7 and H-7 to H-8 (Figure 1). The methylene protons (H-6) of the cyclopentane ring,  $\delta_{\text{H}}$  2.24 (br t) and 2.58 (dd), showed HMBC connections with  $\delta_{\text{C}}$  93.3 (C-5), 43.7 (C-6), 55.8 (C-7) and  $\delta_{\text{C}}$  69.5 (C-4), 93.3 (C-5), 43.7 (C-6), 55.8 (C-7), 62.2 (C-8), respectively. The singlet at  $\delta_{\text{H}}$  3.92 was connected to 162.8 (C-2), 93.3 (C-5), and 55.8 (C-7). The multiplet at  $\delta_{\text{H}}$  4.74 (H-7) and doublet at  $\delta_{\text{H}}$  4.14 (H-8) showed correlations with  $\delta_{\text{C}}$  93.3 (C-5) and  $\delta_{\text{C}}$  43.7 (C-6), 125.0 (C-11), 108.7 (C-14), respectively. As for compound **3**, NOESY experiments of **4** showed clear correlations between H-7 and H-6/H-8, while H-4 does not correlate with any proton. These observations together with the very similar 1D  $^1\text{H}$  NMR spectra of **3** and **4** included in the Supporting Information indicate that the relative configuration of **4** must be the same as for **3**.

The ESI-MS of compound **5** displayed five pseudomolecular ion peaks at  $m/z$  771, 773, 775, 777, and 779  $[\text{M} + \text{H}]^+$ , which indicated the presence of four bromines in the molecule. The molecular formula of **5** was determined to be  $\text{C}_{22}\text{H}_{18}\text{Br}_4\text{N}_{10}\text{O}_2$  by (–)-HRESIMS. The  $^1\text{H}$  NMR spectrum displayed only a few protons at  $\delta_{\text{H}}$  3.43(m)/3.97(dd) for H-8,  $\delta_{\text{H}}$  3.71(dd, H-7), and  $\delta_{\text{H}}$  6.60(d, H-15), suggesting it to be a symmetric molecule. The comparison of the  $^1\text{H}$  NMR spectrum of **5** with the data of

benzosceptrins A (**7**) and B (**8**), recently isolated in our group,<sup>22</sup> suggested it to be a benzosceptrin-type compound with the benzocyclobutane ring system. The <sup>1</sup>H NMR spectra were similar in the upfield region with the difference in the pyrrole proton region. Only a single pyrrole proton peak at  $\delta_{\text{H}}$  6.60 (2H, H-15) was observed. Thus, the molecule differs from benzosceptrins A (**7**) and B (**8**) in the degree of bromination. Interestingly, the chemical shifts of the remaining pyrrolic protons are not dramatically changed with the degree of bromination. Comparison of the chemical shifts of H-13 ( $\delta_{\text{H}}$  8.86), H-14 ( $\delta_{\text{H}}$  6.08), and H-15 ( $\delta_{\text{H}}$  6.61) in benzosceptrin A (**7**)<sup>22</sup> with H-13 ( $\delta_{\text{H}}$  8.86) and H-15 ( $\delta_{\text{H}}$  6.61) in the dibrominated benzosceptrin B (**8**) and the signal at  $\delta_{\text{H}}$  6.60 in **5** clearly show that it corresponds to H-15. Similar chemical shifts have been observed for debromosceptrin,<sup>23</sup> sceptrin, and dibromosceptrin.<sup>24</sup> The <sup>13</sup>C NMR spectrum gave the characteristic values for the brominated carbons at  $\delta_{\text{C}}$  100.3 (C-14) and 106.4 (C-13). The intense signal at  $\delta_{\text{C}}$  114.4 was attributed C-15. This was confirmed by the HMBC correlations of H-15 with C-10 at  $\delta_{\text{C}}$  162.1 and C-11 at  $\delta_{\text{C}}$  128.6. In fact, the HMBC correlations were similar to those observed for benzosceptrin A (Figure 1).<sup>22</sup> The <sup>1</sup>H–<sup>1</sup>H COSY spectrum showed correlations between  $\delta_{\text{H}}$  3.43 (m, H-8a), 3.97 (dd, H-7), and 3.71 (dd, H-8b). The <sup>13</sup>C NMR spectrum gave the corresponding carbon values at  $\delta_{\text{C}}$  49.7 (CH-7) and 43.7 (CH<sub>2</sub>-8).

The specific rotation,  $[\alpha]_{\text{D}}^{25} -22.7$ , showed the C7–C7' *trans* configuration, indicating the preservation of the C<sub>2</sub> symmetry axis like for sceptrin (**6**) and benzosceptrins A and B. A *cis* configuration for C7–C7' would give the achiral *meso* compound. This third remarkable and unique benzocyclobutane metabolite was named benzosceptrin C (**5**).<sup>25</sup>

For biogenetic considerations, we have previously suggested that the agelastatin skeleton could be derived from oroidin through subtle tautomerization and the dual reactivity induced by the 2-aminoimidazole portion of the structure.<sup>14a</sup> A preagelastatin motif like that we have proposed is clearly shown by the dimeric natural product nagelamide J, recently isolated by Kobayashi and co-workers.<sup>26</sup> A discussion regarding the mechanism for formation of the benzosceptrin skeleton has also been reported in our previous paper.<sup>22</sup>

The pure compounds were screened for cytotoxicity against the KB cell line,<sup>27</sup> and except for agelastatin A (**1**) (100% activity at 30 and 3  $\mu\text{M}$ ), all of the compounds lacked significant bioactivity at 30  $\mu\text{M}$ . The pharmacological activities of agelastatin A have been extensively studied.<sup>28</sup> The sharp difference between the high activity of agelastatin A compared to the natural derivatives agelastatins B–F reveals very little flexibility for synthetic analogues and structure–activity relationship studies.

In conclusion, the majority of the compounds isolated from *A. dendromorpha* are of the pyrrole-2-aminoimidazole type. In addition to the known cytotoxic compounds agelastatin A (**1**) and agelastatin D (**2**), which have already been isolated from the same sponge, we have isolated agelastatins E (**3**) and F (**4**). Benzosceptrin C (**5**) was also isolated as a new P-2-AI derivative. Moreover, metabolites having a substituted benzocyclobutane such as benzosceptrin C (**5**), described in this paper, and the benzosceptrins A and B,<sup>22</sup> which we have reported earlier, are completely new. Their significance for chemistry, biology, and chemical ecology is an interesting question. Accordingly, the presence of these compounds should stimulate considerable synthetic interest. It is noteworthy that there are very few examples of benzocyclobutane-containing natural products.

## Experimental Section

**General Experimental Procedures.** Optical rotations were measured in MeOH on a Jasco P1010 polarimeter. The UV spectra were recorded on a Waters 996 photodiode array detector in the HPLC solvent. The IR spectra were measured (neat) on a Perkin-Elmer BX-FT-IR spectrometer. NMR spectra were recorded on Bruker Avance 600 MHz and DRX 500 MHz spectrometers. The chemical shifts were referenced to the residual solvent signal (CD<sub>3</sub>OD,  $\delta_{\text{H}}$  = 3.32,  $\delta_{\text{C}}$  = 49.0). HRMS

data were obtained with a hybrid linear trap/orbitrap mass spectrometer (LTQ-orbitrap, ThermoFisher) in electrospray ionization mode by direct infusion of the purified compounds. Preparative HPLC was performed on an autoprep system (Waters 600 controller and Waters 600 pump with a Waters 996 photodiode array detector). Samples were injected by a Waters 2700 sample manager.

**Sponge Material.** The sponge *Agelas dendromorpha* (order Agelasida, family Agelasidae) was collected during the research cruise Terrasses (October 2008) on a sea mount of the Norfolk rise (23°41' S, 168°00' E), New Caledonia, at a depth of 250 m. The voucher sample is preserved in Muséum National d'Histoire Naturelle in Paris under the accession number ORSTOM-R1569.

**Extraction and Isolation.** The lyophilized sponge *A. dendromorpha* (150 g) was extracted with MeOH (500 mL  $\times$  3). After removing the solvent *in vacuo*, the combined MeOH extract was partitioned between *n*-BuOH (200 mL  $\times$  3) and H<sub>2</sub>O to afford an *n*-BuOH fraction (6.5 g). This *n*-BuOH fraction was chromatographed on a silica gel column (VersaPak, Sigma, 40–150 mm) with gradient elution of MeOH–CH<sub>2</sub>Cl<sub>2</sub> to give 15 subfractions (B1–B15). The alkaloid-rich fractions B8–B15 were further purified on a preparative C18 HPLC (X-bridge column, 19–150 mm), flow rate 17 mL/min, MeOH–0.1% HCOOH and H<sub>2</sub>O–0.1% HCOOH, UV detection at 270 nm. Further purification of the B8 fraction yielded thymine (1.6 mg,  $t_{\text{R}}$  12.2 min), longamide (5.6 mg,  $t_{\text{R}}$  33.1 min), and 4,5-dibromopyrrole-2-carboxamide (6.5 mg,  $t_{\text{R}}$  35.7 min). Fractions B10 and B11 yielded a major compound, agelastatin A (**1**, 380 mg,  $t_{\text{R}}$  31.0 min). The purification of fractions B12–15 afforded three new compounds along with several known compounds, agelastatin D (**2**, 2.0 mg,  $t_{\text{R}}$  26.1 min), agelastatin E (**3**, 1.5 mg,  $t_{\text{R}}$  34.4 min), agelastatin F (**4**, 20.9 mg,  $t_{\text{R}}$  34.1 min), benzosceptrin C (**5**, 0.6 mg,  $t_{\text{R}}$  35.1 min), sceptrin (**6**, 9.3 mg,  $t_{\text{R}}$  17.8 min), manzacidin A (16.0 mg,  $t_{\text{R}}$  29.5 min), tauroacidin A (16.9 mg,  $t_{\text{R}}$  32.7 min), taurodispacamide (37.2 mg,  $t_{\text{R}}$  32.7 min), and nortoposentin D (34.1 mg,  $t_{\text{R}}$  35.7 min). The HPLC (LC-MS) of all the isolated compounds was carried out on an analytical column (Sunfire C18, 5  $\mu\text{m}$ , 4.6–150 mm, flow rate 0.7 mL/min) with an isocratic gradient for 5 min using 98:2 (H<sub>2</sub>O–0.1% HCOOH to MeOH–0.1% HCOOH) followed by a linear gradient to 100% MeOH–0.1% HCOOH in 45 min. The retention time,  $t_{\text{R}}$ , for all the isolated compounds is based on this analytical HPLC.

**Agelastatin A (1):** white solid;  $[\alpha]_{\text{D}}^{25} -58.5$  ( $c$  0.21, MeOH) (lit.<sup>13a</sup> –84.3 ( $c$  0.3, EtOH)).

**Agelastatin D (2):** white solid,  $[\alpha]_{\text{D}}^{25} -12$  ( $c$  0.07, MeOH) (lit.<sup>13b</sup> not given).

**Agelastatin E (3):** white solid;  $[\alpha]_{\text{D}}^{25} -28$  ( $c$  0.09, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 232 (3.95), 286 (4.08); IR (neat)  $\nu_{\text{max}}$  3223, 2933, 1656, 1642, 1552, 1421, 1351, 1197, 1082, 1037  $\text{cm}^{-1}$ ; <sup>1</sup>H and <sup>13</sup>C NMR (CD<sub>3</sub>OD, 600 MHz), Table 1; ESIMS  $m/z$  355, 357 (1:1) [M + H]<sup>+</sup>; HRESIMS  $m/z$  353.0276 [M – H]<sup>–</sup> (calcd for C<sub>13</sub>H<sub>15</sub><sup>79</sup>BrN<sub>4</sub>O<sub>3</sub>,  $m/z$  353.0255).

**Agelastatin F (4):** colorless, amorphous solid;  $[\alpha]_{\text{D}}^{25} -34.3$  ( $c$  0.11, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 208 (4.0), 238 (3.98), 288 (4.18); IR (neat)  $\nu_{\text{max}}$  3254, 1681, 1634, 1552, 1373, 1346, 1221, 1112, 1067  $\text{cm}^{-1}$ ; <sup>1</sup>H and <sup>13</sup>C NMR (CD<sub>3</sub>OD, 600 MHz), Table 1; ESIMS  $m/z$  405, 407, 409 [M + H]<sup>+</sup>; HRESIMS  $m/z$  402.9071 [M – H]<sup>–</sup> (calcd for C<sub>11</sub>H<sub>10</sub><sup>79</sup>Br<sub>2</sub>N<sub>4</sub>O<sub>3</sub>,  $m/z$  402.9048).

**Benzosceptrin C (5):** white solid;  $[\alpha]_{\text{D}}^{25} -22.7$  ( $c$  0.13, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 229 (4.04), 276 (3.90); IR (neat)  $\nu_{\text{max}}$  3156, 1679, 1577, 1565, 1555, 1347, 1228, 1096, 1038, 750, 613  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR (CD<sub>3</sub>OD, 600 MHz) 3.71 (dd,  $J$  = 6.7, 3.8 Hz), 3.97 (dd,  $J$  = 10.1, 3.9 Hz), 3.43 (m), 6.60 (s); <sup>13</sup>C NMR (CD<sub>3</sub>OD, 150.8 MHz) 43.7 (C8, C8'), 49.7 (C7, C7'), 100.3 (C14, C14'), 106.4 (C13, C13'), 114.4 (C15, C15'), 120.2 (C6, C6'), 128.6 (C11, C11'), 154.5 (C2, C2'), 162.1 (C10, C10'), C4 and C5 were not detected; ESI-MS  $m/z$  771, 773, 775, 777, 779; (–)-HRESIMS  $m/z$  768.8301 [M – H]<sup>–</sup> (calcd for C<sub>22</sub>H<sub>18</sub><sup>79</sup>Br<sub>4</sub>N<sub>10</sub>O<sub>2</sub>,  $m/z$  768.8277).

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**Supporting Information Available:** NMR spectra of compounds 1–5 are available free of charge via the Internet at <http://pubs.acs.org>.

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