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Benzosceptrin C, a new dimeric bromopyrrole alkaloid from sponge *Agelas* sp.

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ABSTRACT

A new dimeric bromopyrrole alkaloid possessing a benzocyclobutane ring, benzosceptrin C (**1**), has been isolated from an Okinawan marine sponge of the genus *Agelas* (SS-956), and the structure and relative stereochemistry were elucidated from spectroscopic data. Benzosceptrin C (**1**) showed antimicrobial activity.

Bromopyrrole alkaloids are known to be some of the most common metabolites contained in marine sponges.[1] During our search for bioactive substances from marine organisms, we previously isolated several bromopyrrole alkaloids with unique cyclic skeletons from sponges of the genus *Agelas*.[2–7] Further investigation of extracts of an Okinawan marine sponge of the genus *Agelas* (SS-956) resulted in the isolation of a new dimeric bromopyrrole alkaloid, benzosceptrin C (**1**). Herein we describe the isolation and structure elucidation of **1**.

The sponge *Agelas* sp. (SS-956) collected off Unten-Port, Okinawa, was extracted with MeOH. *n*-BuOH-soluble materials of the extract were subjected to silica gel and C_{18} columns followed by C_{18} HPLC to yield benzosceptrin C (**1**, 0.00036% wet weight) as a colorless amorphous solid together with known related alkaloids, oroidin,[8,9] ageliferin,[10,11] mauritiamine,[12] and nagelamides B,[2] C,[2] L[4], and R.[7]

Benzosceptrin C (**1**) {$[\alpha]_D^{20}$ −5 (*c* 0.5, MeOH)} showed the pseudomolecular ion peaks at *m/z* 771, 773, 775, 777, and 779 (1:4:6:4:1) in the ESIMS, indicating the presence of four bromine atoms, and the molecular formula of **1** was revealed to be $C_{22}H_{18}N_{10}O_2{}^{79}Br_4$ by HRESIMS data [*m/z* 770.8419 $(M+H)^+$, Δ −0.7 mmu]. The UV absorption [λ_{max} 275 nm (ε 16,600)] was attributed to a substituted pyrrole chromophore,[2] while IR absorptions indicated the existence of amino (3414 cm^{-1}) and amide carbonyl (1645 cm^{-1}) functionalities.

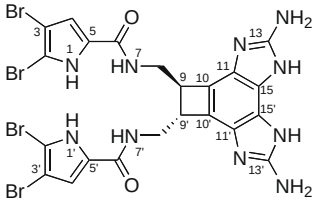

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Table 1
^1H and ^{13}C NMR data of benzosceptrin C (**1**) in DMSO-d_6

Position	δ_H	δ_C
1,1′	12.50 (s)	–
2,2′	–	104.5 (s)
3,3′	–	97.9 (s)
4,4′	6.81 (s)	112.8 (d)
5,5′	–	128.0 (s)
6,6′	–	159.2 (s)
7,7′	8.15 (br s)	–
8,8′	3.84 (m), 3.48 (m)	40.5 (t)
9,9′	3.62 (m)	46.8 (d)
10,10′	–	121.5 (s)
11,11′[a]	–	120.9 (s)
12,12′[b]	–	–
13,13′	–	150.8 (s)
14,14′[b]	6.74 (s)	–
15,15′[a]	–	115.0 (s)
13,13′-NH_2	8.46 (s)	–

[a,b] Exchangeable.

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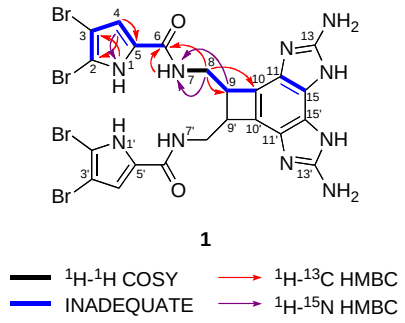

Figure 1. Selected 2D NMR correlations for benzosceptrin C (**1**).

Table 2
Antimicrobial activities of benzosceptrin C (**1**)

Strain	MIC (μg/mL)
Bacillus subtilis	13.0
Escherichia coli	13.0
Micrococcus luteus	6.0
Stapylococcus aureus	13.0
Trichophyton mentagrophytes	6.0
Cryptococcus neoformans	13.0
Candida albicans	13.0
Aspergillus niger	13.0

The ^{13}C NMR data disclosed eleven signals due to an amide carbonyl (δ_C 159.2), seven sp^2 quaternary carbons (δ_C 150.8, 128.0, 121.5, 120.9, 115.0, 104.5, and 97.9), and one sp^2 methine (δ_C 112.8), one sp^3 methine (δ_C 46.8), and one sp^3 methylene (δ_C 40.5) (Table 1). These data and the molecular formula of **1** indicated that **1** was a symmetric, dimeric bromopyrrole alkaloid. Among eleven carbon signals, three sp^2 quaternary carbons (δ_C 128.0, 104.5, and 97.9) and one sp^2 methine (δ_C 112.8) were ascribed to a 5-monosubstituted 2,3-dibromopyrrole ring (N-1–C-5), while three sp^2 quaternary carbons (δ_C 150.8, 120.9, and 115.0) were assigned to a 4,5-disubstituted 2-aminoimidazole ring (C-11–C-15) by comparison of ^{1}H and ^{13}C NMR data of **1** (Table 1) with those of known bromopyrrole alkaloids.[2–7]

The ^{1}H–^{1}H COSY and INADEQUATE spectra of **1** disclosed the connections for C-2 to C-6, N-7 to C-10, and C-11 to C-15. ^{1}H–^{13}C HMBC correlations for NH-1/C-3, H-4/C-2, and H-4/C-5, and a ^{1}H–^{15}N HMBC correlation for H-4/N-1 supported the presence of a 5-monosubstituted 2,3-dibromopyrrole ring (N-1–C-5). Connectivities of C-5 and C-8 through an amide bond were revealed by ^{1}H–^{13}C HMBC cross-peaks of H$_2$-8/C-6 and NH-7/C-6. ^{1}H–^{15}N HMBC correlations for H-8/N-7 and H-9/N-7 also supported the connectivities from N-7 to C-9 (Fig. 1). Considering the molecular formula of **1**, it was deduced that C-10 was connected to C-11 or C-15 of a 4,5-disubstituted 2-aminoimidazole ring (C-11–C-15). Since **1** was considered to be a symmetric molecule, the gross structure of benzosceptrin C (**1**) was elucidated to be as shown in Figure 1. The relative configuration for H-9 and H-9′ was assigned as trans, since benzosceptrin C (**1**) is optically active and should have C2 symmetry axis.

Benzosceptrin C (**1**) is a new dimeric bromopyrrole alkaloid possessing a benzocyclobutane ring. Several proposals for biogenetic path of sceptrin[13] and its related alkaloids have been reported so far.[14–17] Benzosceptrin C (**1**) might be derived from two molecules of oroidin[8,9] through dibromosceptrin[18] (Fig. 2). Benzosceptrin C (**1**) showed antimicrobial activities against some bacteria and fungi as shown in Table 2.

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Supplementary data

Supplementary data (NMR spectra of **1**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.10.017.

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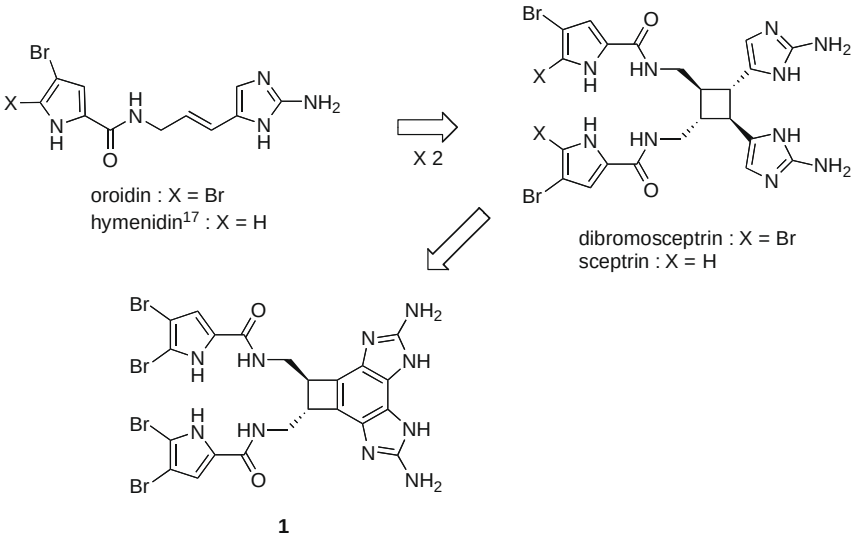

Figure 2. Plausible biogenetic path for benzosceptrin C (**1**).

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