11,17-Dideoxyagelorin A and B, New Bromotyrosine Derivatives and Analogs from the Marine Sponge *Suberea* aff. *praetensa*

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Suberea aff. *praetensa*, 11-Dideoxyagelorin A and B, Bromotyrosine Derivatives

A collection of the marine sponge *Suberea* aff. *praetensa* from the Gulf of Thailand furnished the bromotyrosine derivatives fistularin-3, agelorins A and B and the new desoxyagelorins A and B.

Introduction

All sponge genera of the order Verongida (class Demospongia, subclass Ceractinomorpha) which have so far been examined chemically contain secondary metabolites derived from bromo- or chlorotyrosine in which the side chain has been converted into a variety of nitrogenous groups while the aromatic ring has been retained or has undergone rearrangement or reduction (Bergquist and Wells, 1980). A subclass of these metabolites consist of compounds such as the fistularins (Gopichand and Schmitz, 1979) in which one or two modified tyrosine moieties are attached to a chain consisting of variously modified 3,5-dibromo-4-(γ-amino propoxy)-phenylethyl amines (Cimino *et al.*; 1983, Kernan *et al.*, 1990; Gunasekera and Cross, 1992; Ciminiello *et al.*, 1994, 1996, 1997; Compagnone *et al.*, 1999). The first and so far only bromotyrosine derivatives isolated from a non-verongid sponge were the agelorins A (**1a**) and B (**1b**) found (Koenig and Wright, 1993) together with 11-epifistularin B in *Agelas oroides* (Demospongia, subclass Tetractinomorpha, order Axinellida, family Agelasidae). We now report isolation from a Gulf of Thailand collection of *Suberea* aff. *praetensa* (Demospongia, Ceractinomorpha, Verongida, family Aplysinellidae) of the agelorins A and B, the new 11,17-dideoxyagelorins A and B (**2a** and **2b**) and the related, fistularin-3 (Gopichand and Schmitz, 1979) as well as clionasterol.

Materials and Methods

^{1}H and ^{13}C NMR spectra were recorded at ambient temperature on a Bruker AMC instrument operating at 300.13 and 75.47 MHz, respectively. EI mass spectra were measured on a Hitachi Perkin-Elmer RMV-6M instrument. For HRMS samples were run using +FAB ionization with Xe gas at 6KV on a KRATUS CONCEPT III, 2 sector mass spectrometer. The accelerating voltage was 8 KV. Silica gel for column chromatography was Si gel 60 (0.2–0.5 mm) Merck, for analytical and preparative TLS Si gel G-60 GF 254 Merck.

Animal material

Suberea aff. *praetensa* was collected from a trawl net on the seashore of Ban Phae village on the Gulf of Thailand, Rayong Province, Thailand, in March 1998. The sponge was identified by Prof. Rob van Soest, Department of Coelenterates and Porifera, Zoological Museum, University of Amsterdam. A voucher (BIMS-1954) was deposited

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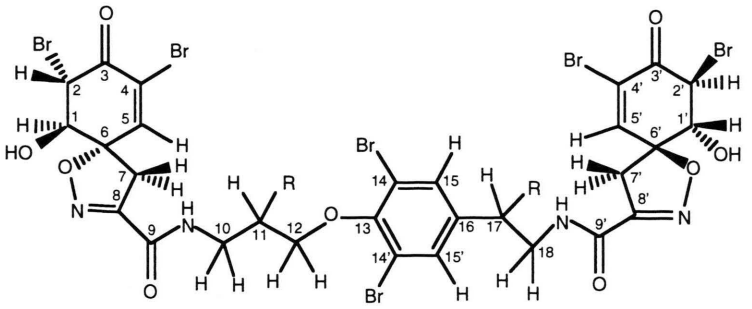
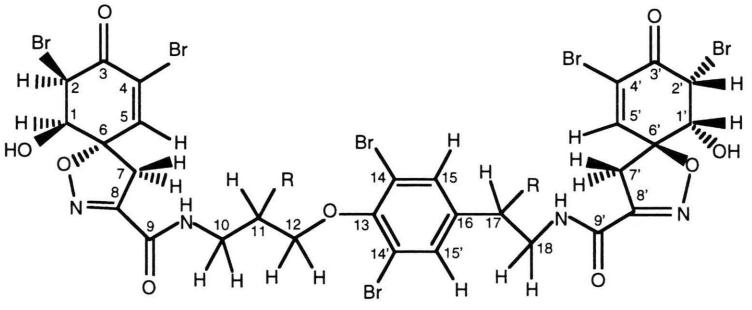


1a R = OH Agelorin A
2a R = H



1b R = OH Agelorin B
2b R = H

at the Reference Collection Museum of the Institute of Marine Science, Burapha University, Bangsaen, Chonburi, Thailand. The collected material was immediately frozen at −20º C for one night prior to extraction.

Extraction and isolation of the constituents

The sample (164 g net weight) was thawed, homogenized with EtOH (500 ml), allowed to stand in a dark chamber for 24 hours and filtered. The residue on the filter paper was again extracted with EtOH (3 × 500 ml). The aqueous alcoholic extracts were combined, evaporated at reduced pressure until the final volume of the aqueous solution was ca. 100 ml and extracted with EtOAc (3 × 300 ml). The EtOAc extracts were combined and concentrated at reduced pressure to give a residue (3.4 g). The latter was chromatographed over Si gel (50 g) and eluted with petrol-$CHCl_3$, $CHCl_3$-Me_2O and $CHCl_3$-MeOH, 125 ml frs being collected as follows: frs 1–27 (petrol-$CHCl_3$, 4:1), 28–46 (petrol-$CHCl_3$, 3:2), 47–71 (petrol-$CHCl_3$, 2:3), 72–86 (petrol-$CHCl_3$, 1:4), 87–98 ($CHCl_3$), 99–145 ($CHCl_3$-Me_2O, 9:1), 146–160 ($CHCl_3$-Me_2O, 7:3), 161–177 ($CHCl_3$-Me_2O, 1:1), 178–189 ($CHCl_3$-MeOH, 9:1). The ratios refer to v/u.

Frs 5–8 (210 mg) were recrystallized from petrol to give clionasterol (176 mg) identified by MS and ^1H NMR spectrometry. Frs 54–59 (29 mg) were purified by TLC (Si gel, $CHCl_3$-petrol-EtOAc, 8:1:1) to give 1-hexene (12 mg). Frs 70–80 (54 mg) on purification by TLC (Si gel, $CHCl_3$-MeOH-HCO_2H, 85:15:0.5) gave a non-crystalline mixture of 11,17-dideoxyagelorin A and B (28 mg). Frs 105–144 (230 mg) were purified by

TLC (Si gel, $CHCl_3$-Me_2OH-HCO_2H, 70:30:1) to give fistularin-3 (120 mg) and a non-crystalline mixture of agelorin A and agelorin B (70 mg). Fistularin-3 was identified by HRMS, ^1H and ^{13}C NMR measurements (^1H, ^{13}C, NOESY, HMBC), conversion to the tetraacetate, ^1H and ^{13}C NMR measurements of the latter and comparison of the data with the literature (Gopichand and Schmitz, 1979; Gunasekera and Cross, 1992; Campagnone *et al.*, 1999). No attempt was made to separate the mixture of agelorin A (**1a**) and agelorin B (**1b**) whose structures were confirmed by HRMS and extensive ^1H and ^{13}C NMR measurements (^1H , ^{13}C, COSY, HMBC) in DMSO solution for comparison with the mixture of new dideoxy derivatives **2a** and **2b**.

11,17-Dideoxyagelorins A and B (2a and 2b). Due to the small amount of material no attempt was made to separate the noncrystalline mixture, + FAB-HRMS (NBA) M + H^+ 1054.68209; calcd. for $^{12}C_{29}\,^1H_{27}\,^{14}N_4\,^{16}O_9\,^{79}Br_3\,^{81}Br_3$ 1054.68207. ^1H and ^{13}C NMR spectra are listed in Table I, assignments being based on decoupling, COSY and HMBC correlations. Comparison with the ^1H and ^{13}C NMR spectra of the agelorin A-agelorin B mixture under the same conditions established identity except for the absence of the hydroxyl groups at C-11 and C-17.

Discussion

As mentioned earlier brominated metabolites derived from tyrosine have so far been found only in sponges of the order Verongida, the exception being *Agelas oroides*. The only previous report on the chemistry of a *Suberea* species mentions the occurrence of the bromotyrosine derivatives (+) aerothonin, homoaerothonin, (+) aeroplysinin-1 and haloverongiaquinols in *Suberea creba* from the Coral Sea (Debitus *et al.*, 1998).

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Table I. ^1H and ^{13}C NMR spectra of 11,17-dideoxyagelorins A and B[a].

Position	δH(mult)A,A′[b]	δC(mult)A,A′[c]	δH(mult)B,B′[b]	δC(mult)B,B′[c]
1,1′	4.18 *d* (11,4)	73.34 *d*, 73.29 *d*	4.29 *brs*	72.01 *d*
2,2′	5.19 *dd* (11,3)	57.81*d*	5.35 *m*	55.84 *d*
3,3′		183.81 *s*		183.39 *s*
4,4′		121.34 *s*, 121.31 *s*		122.75 *s*
5,5′	*7.68 s*, 7.65 *s*	149.06 *d*, 148.97 *d*	7.54 *s*	145.35 *d*
6,6′		90.51 *s*		89.38 *s*
7a, 7′a	3.65 *d*(18), 3.63 *d*(18)	38.03 *t*	3.65 *d*(18), 3.63 *m*	38.03 *t*, 39.79 *t*
7b, 7′b	*3.13* *d*(18), 3.10 *d*(18)		3.33 *d* (18), 3.30 *d*(18)	
8,8′		153.92 *s*, 153.89 *s*		154.57 *s*, 153.92 *s*
9,9′		158.85 *s*[d]		158.78 *s*[d]
10a,b	3.42 *m*	36.31 *t*	3.42 *m*	36.31 *t*
11a,b	*2.00* *q*(6)	29.62 *t*	2.00 *q*(6)	29.62 *t*
12a,b	3.95 *dd*(6,4)	71.24 *t*	3.95 *dd* (6,4)	71.24 *t*
13		150.75 *s*		150.75 *s*
14		117.38 *s*		117.38 *s*
15,15′	7.53 *s*	133.04 *d*	7.53 *s*	133.04 *d*
16		133.88 *s*		133.88 *s*
17a,b	2.76 *t*(7)	33.20 *t*	2.76 *t*(7)	33.20 *t*
18a,b	3.42 *m*	39.79 *t*	3.42 *m*	39.79 *t*
NH_a	8.67 *dd* (11.8,5.7)		8.67	
NH_b	8.64 *dd* (11.8, 5.7)		8.64	
OH	6.77 *br*		6.77 *br*	

[a] From mixture of **2a** and **2b**. A and A′, B and B′ refer to the left and right halves of the structures of A and B. Spectra recorded in DMSO-d_6; assignments by HMBC and COSY.
[b] J values in parentheses.
[c] Multiplicities deduced by DEPT.
[d] Assignments may be interchanged.

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