Annonacin (**II**) was obtained as a whitish wax with m.p. 57 °C. The molecular formula of annonacin was established by high resolution CIMS, and the IR, $^{13}C$ NMR and $^{1}H$ NMR spectra were identical to the published values for annonacin[6]. Co-TLC with an authentic sample of annonacin in five different TLC systems and optical rotations ($\alpha_D$ + 1.4 °) showed complete homogeneity, indicating that the two isolates were identical.

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## 1,1-Dimethyl-5,6-dihydroxyindolinium chloride from a deep water marine sponge, *Dercitus* sp.

S. Kohmoto, O. J. McConnell[1,2] and A. Wright

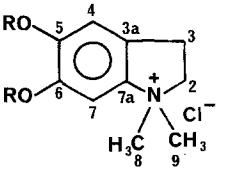
*Harbor Branch Oceanographic Institution, Inc./SeaPharm Project, 5600 Old Dixie Highway, Ft. Pierce (Florida 33450, USA),*
*11 June 1987*

*Summary.* 1,1-Dimethyl-5,6-dihydroxyindolinium chloride (**1a**) was identified from a deep water sample of the marine sponge, *Dercitus* sp., and its structure was elucidated by spectral methods.
*Key words.* 1,1-Dimethyl-5,6-dihydroxyindolinium chloride; marine natural products; *Dercitus*; marine sponge.

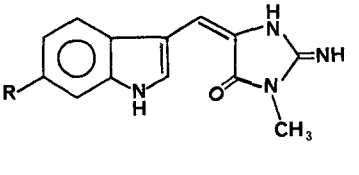
Numerous nitrogen-containing metabolites have been isolated from marine sponges[3–5], but only a small percentage of these metabolites contain a quaternary ammonium functionality. In this note, we report the isolation and identification of 1,1-dimethyl-5,6-dihydroxyindolinium chloride (**1a**), a new marine natural product from a deep water sponge, *Dercitus* sp. Gray, 1867[6]. Two tryptophan derivatives, 2'-de-N-methyl-aplysinopsin (**2a**) and 6-bromo-2'-de-N-methyl-aplysinopsin (**2b**), have been reported from a shallow water sample of *Dercitus* sp.[7].

The sponge was collected northwest of Goulding Cay, Bahamas, in August, 1985, at a depth of 215 m using the Harbor Branch Oceanographic Institution's submersible, the Johnson Sea-Link II. Sequential solvent extraction of the fresh frozen sponge (97 g) with EtOAc and MeOH yielded crude extracts (0.15 g and 2.7 g, respectively). From a portion of the MeOH extract (2 g), **1a** (118 mg) was purified with multilayer planetary coil CCC[8] using a solvent system of $CHCl_3$–MeOH–$H_2O$ (5/10/6), followed by recrystallization from MeOH–$CHCl_3$ (m.p. 244 °C).

The molecular formula of **1a** was deduced as $C_{10}H_{14}NO_2Cl$ from elemental analysis of the monohydrate of the chloride salt (calculated for $C_{10}H_{16}NO_3Cl$: C, 51.5; H, 6.86; N, 6.00; Cl, 15.0; found: C, 51.58; H, 6.96; N, 6.02; Cl, 15.62) and high resolution FABMS (m/z of $C_{10}H_{14}NO_2$, 180.1021, $\Delta$ 0.4 nm). The presence of a 1,2,4,5-tetrasubstituted benzene ring in **1a** was suggested by the $^{1}H$ NMR singlets ($d_4$-MeOH) at $\delta$ 6.81 (H-4) and 7.09 (H-7), the chemical shifts and multiplicities of the $sp^2$ carbons (from proton decoupled and DEPT $^{13}C$ NMR experiments in $d_4$-MeOH: $\delta$ 124.9 (C-3a, s), 112.5 (C-4, d), 149.5 (C-5, s), 147.7 (C-6, s), 104.4 (C-7, d), and 139.5 (C-7a, s), and the relationship of these $^{13}C$ NMR doublets with the $^{1}H$ NMR singlets (from a C–H correlation experiment[9]). The presence of two phenolic hydroxyls in **1a** was suggested by the $^{13}C$ NMR singlets with chemical shifts of $\delta$ 147.7 and 149.5, IR bands at 3360 and 3140 $cm^{-1}$, the absence of a carbonyl band in the IR spectrum, and the formation of a diacetate (**1b**) upon treatment of **1a** with pyridine and acetic anhydride (**1b**:




**1a**, R = H
**1b**, R = Ac




**2a**, R = H
**2b**, R = Br

LREIMS, m/e 249 (10%, $M^+ - CH_3$), $^1H$ NMR singlets at $\delta$2.30 and 2.31 (3 H each), $^{13}C$ NMR signals at $\delta$169.5 (s × 2) and 20.3 (q × 2), and an IR band at 1775 $cm^{-1}$). As expected for phenols, a bathochromic shift was observed in the UV spectrum upon addition of base ($\lambda_{max}$ (MeOH, nm) 206 ($\varepsilon$ 12 200), 223 (sh, $\varepsilon$ 3800) and 289 ($\varepsilon$ 3700) shifted to 209 ($\varepsilon$ 16 500), 248 ($\varepsilon$ 5800) and 303 ($\varepsilon$ 5100)). Still to be accounted for are 10 protons, 4 carbons and 1 nitrogen. Based on the remaining $^{13}C$ and $^1H$ NMR data ($\delta$ 3.45 (6 H, s)/55.3 (q), 3.25 (2 H, t, J = 7.2)/27.5 (t) and 4.15 (2 H, t, J = 7.2)/(70.0 (t)), the final partial structure in **1a** must be N,N,N-dimethylethylamine where the nitrogen and $\beta$-carbon of the ethyl group are attached to ortho positions on the aromatic ring. Complete carbon assignments in the aromatic ring were made based on a long range C–H correlation NMR experiment (J = 10 Hz) which emphasizes three-bond coupling (H 8 and H 9 ($\delta$ 3.45) – C 2 (70.0), C 7a (139.5); H 2 (4.15) – C 8 and C 9 (55.3), C 3a (124.9); H 3 (3.25) – C 4 (112.5); H 4 (6.81) – C 6 (147.7), C 7a (139.5); H 7 (7.09) – C 3a (124.9), C 5 (149.5)). Assemblage of the partial structures suggested by these data yields 1,1-dimethyl-5,6-dihydroxyindolinium chloride as the proposed structure **1a**, and the corresponding diacetate as **1b**.

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## α-Adrenoceptor blocking action of hymenin, a novel marine alkaloid

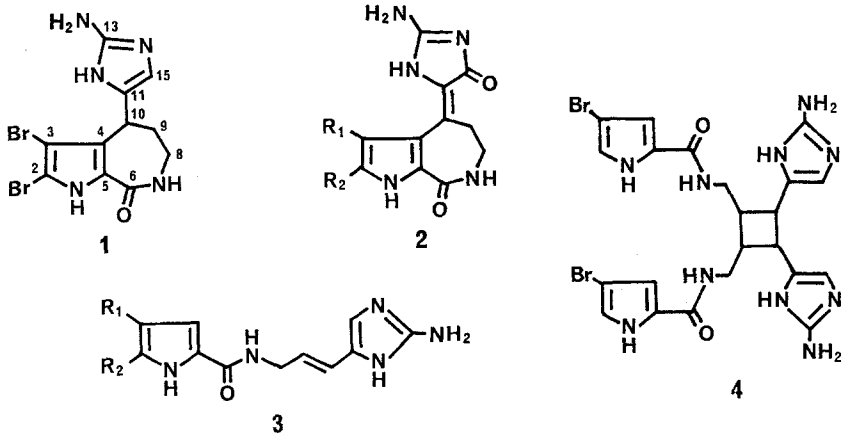
J. Kobayashi*, H. Nakamura and Y. Ohizumi

*Mitsubishi-Kasei Institute of Life Sciences, 11 Minamiooya, Machida-shi, Tokyo 194 (Japan), 29 June 1987*

*Summary.* In the rabbit isolated aorta, hymenin ($10^{-6}$ M), a novel marine alkaloid, caused a parallel rightward shift of the dose-response curve for norepinephrine without affecting that for histamine or KCl, suggesting that hymenin is a competitive antagonist of α-adrenoceptors in vascular smooth muscles.
*Key words.* α-Blocking action; hymenin; aorta; marine alkaloid; antagonist.

Marine organisms have proved to be a good source of compounds useful as tools for pharmacological, physiological and biological studies, since they act on specific sites in the cell membrane[1–4]. During our survey of marine natural products isolated by bioassay-guided purification, we have focused on compounds with α-adrenoceptor blocking activity because of their important role in basic and clinical pharmacology[5, 6]. Recently, a novel bromopyrrole compound, named hymenin (**1**), has been isolated as a potent α-adrenoceptor blocker from a marine sponge[7]. The present study was carried out to characterize the pharmacological properties of hymenin (**1**) and its related compounds (**2a, 2b, 3a, 3b** and **4**) as shown in figure 1.

Male Wistar rats (250–300 g) were anesthetized with sodium pentobarbital (50 mg/kg, i.p.). The right carotid artery was cannulated for arterial blood pressure monitoring, and the blood pressure was continuously recorded by means of a pressure transducer on a polygraph. Drugs were administered via a cannulated right jugular vein. Male albino rabbits (2–3 kg) were killed by a blow on the head. The thoracic aorta was excised and mounted vertically in a 20-ml organ bath containing a Krebs-Ringer-bicarbonate solution of the following composition (mM): NaCl, 120; KCl, 4.8; $CaCl_2$, 1.2; $MgSO_4$, 1.3; $KH_2PO_4$, 1.2; $NaHCO_3$, 25.2, and glucose, 5.8, at pH 7.4, and were continuously gassed with 95% $O_2$ and 5% $CO_2$. The aorta was cut to form a helical strip as described previously[8]. Contractile force was recorded isometrically on a pen recorder. The following drugs were used in the present study: norepinephrine bitartrate (Sigma), histamine dihydrochloride (Wako Pure Chemical) and sodium



**1** : Hymenin
**2a**: Hymenialdisine $R_1$ = H, $R_2$ = Br
**2b**: Debromohymenialdisine $R_1$ = $R_2$ = H
**3a**: Oroidin $R_1$ = $R_2$ = Br
**3b**: Hymenidin $R_1$ = Br, $R_2$ = H
**4** : Sceptrin

Figure 1. Structures of hymenin (**1**) and its related compounds (**2a–4**) isolated from the sponge *Hymeniacidon* sp.