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Sagitol, A Pyridoacridine Alkaloid from the Sponge *Oceanapia sagittaria*

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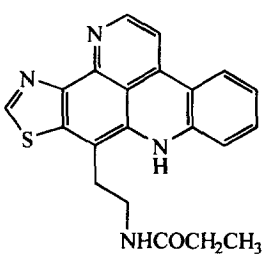
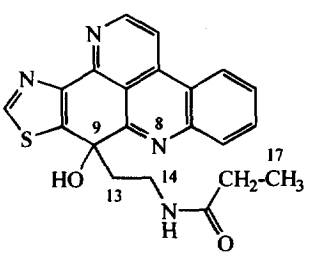
Abstract: The sponge *Oceanapia sagittaria* from Palau contained the known sponge metabolite dercitamide (**1**) and a new pyridoacridine alkaloid sagitol (**2**). The structure of sagitol (**2**) was determined by interpretation of spectral data and confirmed by oxidation of dercitamide (**1**). CD measurements suggest that sagitol (**2**) is not an artifact.

The pyridoacridine alkaloid dercitamide, a metabolite of the deep water sponge *Stelletta* sp., was first reported in 1989.[1] In 1992 the structure was revised when it was shown that dercitamide (**1**), isolated from a tunicate of the genus *Cystodytes*,[2] was identical to kuanoniamide C, previously isolated from an unidentified tunicate and its mollusc predator *Chelynotus semperi*.[3] Unlike most marine natural products, it is not unusual for pyridoacridine alkaloids to be found in different marine phyla and this has led to speculation about their biosynthetic origins.[4] Two competing hypotheses are that these alkaloids are produced by symbiotic microorganisms or that the same biosynthetic pathway has evolved independently in different phyla.[5] As part of a project to study the cellular localization of the pyridoacridine alkaloids, we isolated dercitamide (**1**) as the major metabolite of *Oceanapia sagittaria*. In this paper we report the structural elucidation of a minor metabolite, sagitol (**2**).



(**1**)



(**2**)

Specimens of the sponge *Oceanapia sagittaria*[6] were collected by hand at Ngeruktebel marine lake (-4 m) in Palau and were kept frozen until extraction. The CH_2Cl_2 soluble material from a MeOH extract of *O. sagittaria* was chromatographed on Sephadex LH-20 (MeOH) then C_{18} silica (1:1 MeOH/H2O - MeOH) to obtain dercitamide (**1**, 0.8% dry wt.) and sagitol (**2**, 0.016% dry wt.).

Sagitol (**2**) was isolated as a yellow glass.[7] The molecular formula, $C_{21}H_{18}N_4O_2S$, contained one more oxygen atom than that of dercitamide (**1**) and the IR spectrum suggested the presence of an alcohol (3280 cm^{-1}). The presence of a tertiary alcohol was confirmed by a ^1H NMR signal at δ 4.60 (br s, -OH) and a ^{13}C NMR signal at 74.1 (s). HMBC correlations between the ^{13}C NMR signal at δ 74.1 and the side chain proton signals at δ 3.11 (m, 2 H, H-13), 2.47 (m, 1 H, H-14) and 2.38 (m, 1 H, H-14) serve to locate the tertiary alcohol at C-9. A strong hydrogen bond between the amide NH and N-8 causes the H-14 proton signals to be stereotopic and forces the ethyl group to reside in the ring current of the quinoline ring system, which shifts the ethyl signals upfield to δ 0.94 (t, 3 H) and 1.92 (q, 2H) from their "normal" positions at 1.39 (t, 3 H) and 2.79 (q, 2H) in dercitamide (**1**).

The structure of sagitol (**2**) was confirmed by autoxidation of dercitamide (**1**) with singlet oxygen [O_2, hυ, MeOH, 16 hr.] to obtain a mixture of oxidation products, one of which was sagitol (**2**, 4% yield). Whereas the synthetic sample of sagitol (**2**) was racemic, the CD spectrum of the natural material showed weak positive [262 nm ($\Delta\epsilon$ +0.066)] and negative [312 nm ($\Delta\epsilon$ -0.052)] Cotton effects, suggesting that the natural material was not an artifact of the isolation procedure. Sagitol (**2**) is the first pyridoacridine alkaloid from a marine sponge in which the aromatic system has been disrupted.[8]

References and notes.

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2. Gunawardana, G.P.; Koehn, F.E.; Lee, A.Y.; Clardy, J.; He, H.; Faulkner, D.J. *J. Org. Chem.* **1992**, *57*, 1523.
3. Carroll, A.R.; Scheuer, P.J. *J. Org. Chem.* **1990**, *55*, 4426.
4. Molinski, T.F. *Chem. Rev.* **1993**, *93*, 1825.
5. Faulkner, D.J.; He, H.; Unson, M.D.; Bewley, C.A.; Garson, M.J. *Gazz. Chim. Ital.* **1993**, *123*, 301.
6. A specimen of *Oceanapia sagittaria* (95-061) has been deposited in the SIO Benthic Invertebrate Collection (P-1163).
7. Sagitol (**2**): yellow glass; IR (film) 3280, 2930, 1645, 1600, 1560, 1450 cm^{-1}; UV (MeOH) 396 nm (ϵ 1470), 351 nm (ϵ 3430), 335 nm (ϵ 3920), 318 nm (ϵ 3430), 260 nm (ϵ 22810); ^1H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, 3 H, *J* = 7.5 Hz), 1.92 (q, 2 H, *J* = 7.5 Hz), 2.38 (m, 1 H), 2.47 (m, 1 H), 3.11 (m, 2 H), 4.60 (brs, -OH), 5.57 (br s, 1 H), 7.81 (t, 1 H, *J* = 8.5 Hz), 7.93 (t, 1 H, *J* = 8 Hz), 8.27 (d, 1 H, *J* = 8 Hz), 8.29 (d, 1 H, *J* = 8 Hz), 8.59 (d, 1 H, *J* = 8.5 Hz), 9.04 (s, 1 H), 9.05 (d, 1 H, *J* = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.5 (t), 29.4 (d), 35.2 (d), 47.4 (d), 74.1 (s), 114.0 (s), 114.7 (d), 122.1 (s), 123.0 (d), 128.3 (d), 130.1 (d), 131.5 (d), 138.2 (s), 142.0 (s), 144.9 (s), 148.3 (s), 149.5 (s), 149.9 (d), 154.6 (d), 161.5 (s), 173.6 (s); EIMS *m/z* (int.) 390 (1, M^+), 290 (100); HRCIMS, Obsd. *m/z* = 391.1241, $C_{21}H_{19}N_4O_2S$ $[M+H]^+$ requires *m/z* = 391.1229.
8. The sponge was collected by Larry Sharon and Mary Kay Harper, who also did the identification. We thank the Marine Resources Division, Republic of Palau, for a collecting permit. The research was supported by a grant from the National Science Foundation (CHE 95-27064).

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