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Shoki ONAGA,[a] Nicole J. de Voogd[b] and Junichi TANAKA[a]

[a]Department of Chemistry, Biology and Marine Science, Faculty of Science,
University of the Ryukyus, Senbaru 1, Nishihara, Okinawa 903-0213, Japan

[b]Environmental Biology Department, Institute of Environmental Sciences, CML, Leiden University
Einsteinweg 2, 2333 CC Leiden, The Netherlands

Abstract

A new mycalenitrile **1** was isolated from a lipophilic extract of the sponge *Mycale* sp. The structure of **1** was elucidated to be an analog of mycalenitriles by analyzing spectroscopic data and by comparing them with those reported. The olefinic position was estimated by observing a product ion in the MS/MS spectrum.

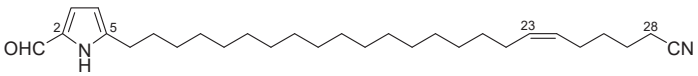
Introduction

Many marine alkaloids contain various structural classes of molecules with biological activity.[1] Among them, pyrrole alkaloids constitute distinct groups.[2] One of the minor pyrrole alkaloids having a C_1 unit at C-2 and an alkyl group at C-5 constitute a small group of pyrrole alkaloids. The first members of this class of molecules[3] were isolated from a sponge *Laxosuberites* sp., followed by a number of analogs.[4,5]

In 2022, the first author was assigned to analyze chemical constituents of a lipophilic extract of a red sponge for his undergraduate thesis research. He isolated compound **1** and characterized a new analog of the above class alkaloid after analyzing spectroscopic data. In this short note, the structure of the new compound **1** is described.

Results and Discussion

A specimen of a sponge *Mycale* sp. collected at Iriomote Island was extracted, and its lipophilic extract was subjected to chromatographic separation to give a conventional steroid and compound **1** which is the subject of this note.



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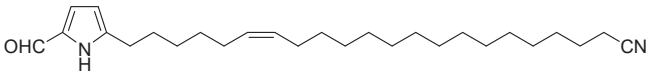

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Figure 1. Structures of compounds **1** and **2**

The molecular formula of **1** was found to be $C_{29}H_{48}N_2O$ by ESIMS. Both ^1H and ^{13}C NMR spectra indicated the presence of several functionalities including an aldehyde (δ 9.40; δ 178.1), a disubstituted pyrrole (δ 6.09 dd, 6.90 dd; δ 109.4~143.2) and a disubstituted double bond (δ 5.34 m (2H); δ 129.4, 130.2). The remaining nitrogen atom was assigned to be a nitrile (δ 119.9; 2246 cm^{-1}). Other structural units consisting of methylenes appeared at different chemical shifts (δ 1.45 m, 1.68 m, 2.04 m, 2.35 t, and 2.64 dt) in addition to large methylene signals at δ 1.27~1.40

and at δ 29.3~29.6. After database search, we found a similar molecule to **1**, namely mycalenitrile-16 (**2**) containing the above functionalities.[5]

By observing HSQC and HMBC cross peaks, the above structural units were found connected as: H-1/C-2, H-6/C-4,5, H-22,25/C-23,24, H-26/C-28, H-27/C-28,29, and H-28/C-26,27,29 confirming that the basic structural components are the same as those for mycalenitriles.[6,7] However, discrepancies in the spectral data between **1** and reported mycalenitriles indicate that the double bond position must be different. With COSY analysis, correlations between H-26/H-25,27 indicated the possible position of the double bond at C-23,24. Since NMR was not so clear enough to assign the exact position of a long aliphatic chain in the structure, we examined the MS/MS spectrum. As results, the precursor ion at *m/z* 441 $[M+H]^+$ gave product ions at *m/z* 68.0495 (C_4H_6N), 80.0494 (C_5H_6N), 108.0443 (C_6H_6NO), and 413.3887 ($C_{28}H_{49}N_2$). Among them, three product ions at *m/z* 80, 108 and 413 are likely formed through cleavage near the pyrrole ring, but the fragment at *m/z* 68 corresponds to the allylic cleavage near the terminal nitrile group (Figure 2). Therefore, the structure of compound **1** was elucidated to have a double bond at C-23. No biological assay was carried out for compound **1**.

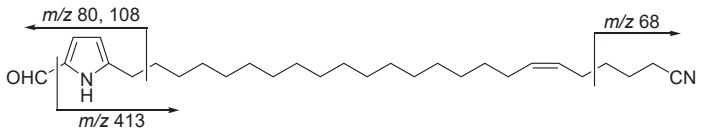

Figure 2. MS/MS product ions

Experimental

General experimental conditions. ^1H and ^{13}CNMR data were measured on a Bruker Avance III spectrometer. ESIMS and MS/MS spectra were obtained on a Waters SYNAPT instrument with positive ESI mode. FTIR spectrum was taken on a Jasco FT/IR-6100 spectrophotometer. Solvents used were reagent grade without distillation.

Extraction and Isolation. A specimen (192 g, wet) of the red sponge *Mycale* sp. growing on a dead coral *Seriatopora* sp. was collected at a coral reef of Funauki Bay, Iriomote Island on July 2012. The genus of the sponge was confirmed by one of us (NJdV).

The sponge was frozen and transferred to laboratory until use. The thawed sponge was extracted with acetone two times, and an ethyl acetate (EtOAc) soluble portion (2.0 g) was obtained.

A portion (1.0 g) was subjected to chromatographic separation on a silica gel column. A fraction eluted with CH_2Cl_2 was concentrated to give 0.18 g of glassy material. The fraction was further separated on reversed phase HPLC (MeOH-EtOAc, 4-1) to give compounds **1** (3.9 mg) and **3** (3.5 mg). After ^1H NMR analysis, compound **3** was found to be a conventional steroid and further study was not done.

Compound 1.

Yellow glass. ^1HNMR ($CDCl_3$) δ 1.27-1.40 (28H, m, H-8~21), 1.45 (2H, m, H-26), 1.68 (4H, m, H-7,27), 2.04 (4H, m, H-22,25), 2.35 (2H, t, J = 7.2 Hz, H-28), 2.64 (2H, dt, J = 2.3, 7.7 Hz, H-6), 5.37 (2H, m, H-23,24), 6.09 (1H, dd, J = 3.7, 2.5 Hz, H-4), 6.90 (1H, dd, J = 3.7, 2.5 Hz, H-3), 9.15 (1H,

br, NH), 9.40 (1H, s, H-1); ^{13}CNMR ($CDCl_3$) δ 17.1 (C-28), 25.4 (C-27), 27.0~27.3 (C-22,25), 27.9 (C-6), 28.7~29.8 (C-6~21,26), 109.4 (C-4), 119.9 (C-29), 122.2 (C-3), 129.4~130.3 (C-23,24), 131.9 (C-2), 178.1 (C-1); FTIR (neat) 3247, 2922, 2851, 2246, 1663, 1639 cm^{-1}; ESIMS obsd *m/z* 441.3832 ($[M+H]^+$, calcd for $C_{29}H_{49}N_2O$ 441.3839).

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