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SYM-TRIAZINE DERIVATIVE FROM *HALIMEDA XISHAENSIS*

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Key Word Index—*Halimeda xishaensis*; alga; *sym*-triazine; halimedin; X-ray diffraction.

Abstract—A 1,3,5-*sym*-triazine derivative, halimedin, was isolated from the alga, *Halimeda xishaensis*. Its structure was established by spectroscopic methods and X-ray crystallographic diffraction analysis. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Sym-triazine-containing compounds possess various biological activities. Synthetic compounds showed antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* [1]. It was also found that the combined presence of N—C=S and thiazole groups in *sym*-triazine nucleus may enhance antibacterial activity [2]. Some synthetic 2,4,6-substituted-*sym*-triazines are anti-microfilarial agents [3]. *Sym*-triazine-containing dicarboxylic acid amino esters exhibit muscarinic cholinomimetic activity [4]. However, thus far, no example of a naturally occurring *sym*-triazine has been found.

In the present work, halimedin (**1**) was isolated from the alga, *Halimeda xishaensis*, which is a new species identified by Tseng and Deng. Halimedin is the first cyano-*s*-triazine derivative isolated from a natural source.

RESULTS AND DISCUSSION

Halimedin (**1**) was assigned the molecular formula $C_{10}H_{16}N_6O$ by FAB-mass spectrometry and elemental analysis. It is a heterocyclic compound with a high N content. The ^{13}C NMR spectrum revealed ten carbon resonances, including four methyl, one methylene and five quaternary carbons. The IR spectrum of **1** exhibited an absorption band at 2242 cm^{-1} and δ_C at 122.7 ppm, indicating the presence of a cyano group. The pattern of its ^{13}C NMR signals in the aromatic carbon region [δ 167.1 (*s*), 167.9 (*s*), 171.7 (*s*)], together with the IR spectrum (3156, 1616, 1581, 1503 and 1461 cm^{-1}) indicated a *s*-triazine nucleus. The remaining two nitrogen atoms were suggested to belong to two amines. IR absorptions at 3325 and 3251 cm^{-1} and the presence of two broad exchangeable signals at δ 7.80 and 8.36 in the ^1H NMR spectrum confirming that there were two NH hydrogens. The NMR signals at δ_C 54.0 (*s*) and δ_H 3.86 (3H, *s*), and the IR absorption at 2820 and 1096 cm^{-1}, indicated the presence of a methoxyl group. The signal of a pair homotopic methyl group at δ_H 1.84 (6H, *s*) and a quaternary carbon at δ_C 28.1, suggested a $(CH_3)_2C$ group. The N-containing methylene (δ_H 3.57, *s*), together with a methyl (δ_H 1.15) comprised an *N*-ethyl group. Thus, the only structure for halimedin, which can satisfy all these data, was deduced as **1**.

To confirm its structure, an X-ray crystallographic analysis was performed. The ORTEP diagram of **1** is shown in (Fig. 1).

EXPERIMENTAL

General

Mps: uncorr. NMR: Bruker Ac-P-200, Py-d_5, using TMS as int. standard.

Plant material

The alga, *H. xishaensis*, was collected from the Xisha Islands in the South China Sea. A voucher specimen (91-24#) is deposited in the Research Center of Organic Natural Products Chemistry, Zhongshan University, Guangzhou, China.

Extraction and isolation

The chopped alga (1.8 kg) was extracted with EtOH at room temp. to give the extract. This was extracted

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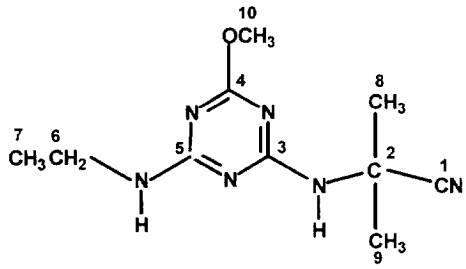

Halimedin (1)

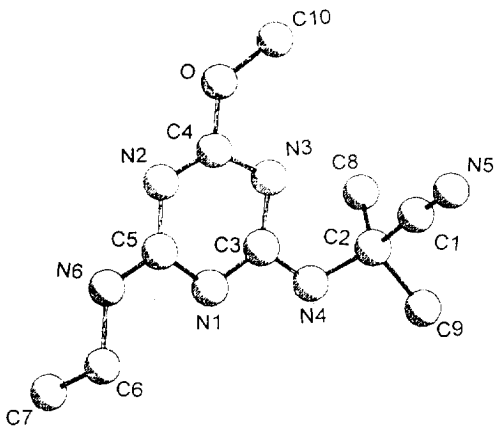

Fig. 1. A perspective view of the structure of halimedin (**1**).

with EtOAc and *n*-BuOH, successively. The BuOH-sol. fr. (2.5 g) was subjected to silica gel CC and then to flash CC over silica gel H eluting with $CHCl_3$ containing increasing amounts of MeOH. The fr. eluted with $CHCl_3$–MeOH (3:1) afforded halimedin (**1**, 50 mg 0.0028%).

Halimedin (**1**). White crystals, mp 164–165°. IR (KBr) ν_{max} 3325, 3251 (NH), 3156, 1616, 1581, 1503, 1461 (triazine nucleus), 2242 (CN), 2820, 1096 (CH_3O), 1382 (*gem*-dimethyl) cm^{-1}. ^1H NMR (200 MHz, Py-d_5): δ 8.36 (1H, NH), 7.80 (1H, NH), 3.86 (3H, *s*, H-10), 3.57 (2H, *m*, H-6), 1.84 (6H, *s*, H-8 and H-9), 1.15 (3H, *t*, J = 6.5 Hz, H-7). ^{13}C NMR (50 MHz, Py-d_5): δ 171.7 (*s*, C-4), 167.9 (*s*, C-3 or C-5), 167.1 (*s*, C-3 or C-5), 122.7 (*s*, C-1), 53.8 (*q*, C-10); δ 29.9 (*t*, C-6), 28.1 (*s*, C-2), 27.9 (*q*, C-8 and C-9), 15.2 (*q*, C-7). FABMS *m/z* (rel. int.): $[M+H]^+$ 237 (100). Elementary analysis (found: C, 50.79; H, 6.99; N, 35.66; $C_{10}H_{16}N_6O$ requires: C, 50.82; H, 6.83; N, 35.58%).

X-ray structure analysis of halimedin (**1**)

Crystal data: $C_{10}H_{16}N_6O$, M_r = 236, orthorhombic, space group *Pcab*, a = 10.029(5) Å, b = 11.152(6)Å, c = 23.783(5) Å, Z = 8, D_c = 1.183 (Mg m^{-3}; λ(Mo–K_α) = 0.71073 Å; μ = 0.08 mm^{-1}, R = 0.070 for 735 observer reflections having $|F|^2 > 10.00\sigma(|F|^2)$. Diffraction data were collected with DIP2000K Inmage Plate diffractometer with a graphite monochromater. Intensities were measured by ω-scans from 0–180° at 1° min^{-1}, the rotation range was 4° and the interval 4°. The distance between the crystal and the IP was 90 mm. A total of 1198 unique reflections were collected, of which 735 were observed. The structure was solved by direct methods, using the SHELXS-86 program. The structure was refined by block-matrix least-squares techniques for all non-hydrogen atoms using 920 reflections having $|F|^2 > 2.5\sigma(|F|^2)$. Coordinations and isotropic parameters of the hydrogen atoms were not refined and the final R was 0.070.

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