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(*S*)-(−)-3,4-DIHYDROXYBUTANOIC ACID γ-LACTONE FROM PUERTO RICAN *LYNGBYA MAJUSCULA*

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Key Word Index—*Lyngbya majuscula*; Oscillatoriaceae; 4(*S*)-hydroxy-2(3*H*)-dihydrofuranone.

Abstract—(*S*)-(−)-3,4-Dihydroxybutanoic acid γ-lactone, which has the opposite configuration of the lactone generated from hydrolysis of oscillatoxin A, is a metabolite of Puerto Rican *Lyngbya majuscula*.

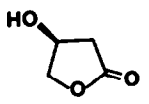
INTRODUCTION

Debromoaplysiatoxin is a potent tumour promoter which is found in certain varieties of the marine blue–green alga *Lyngbya majuscula* from the Hawaiian Islands [1], Enewetak Atoll [2], and Okinawa [3]. The 31-nor compound, oscillatoxin A, which is also a potent tumour promoter [4], is present along with debromoaplysiatoxin in a mixture of two blue–green algae found on the seaward side of Enewetak Island, viz. *Schizothrix calcicola* and *Oscillatoria nigroviridis* [5, 6]. Both debromoaplysiatoxin and oscillatoxin A have the same absolute stereochemistry [6]. The configuration at C-29 in both toxins is *R*. We report here the isolation and identification of (*S*)-(−)-3,4-dihydroxybutanoic acid γ-lactone (**1**) from a non-toxic variety of *L. majuscula* found abundantly at Mayaguez, Puerto Rico. This γ-lactone has the opposite absolute stereochemistry from the one obtained from chemical degradation of oscillatoxin A.

RESULTS AND DISCUSSION

Fractionation of the algal extract led to the isolation of compound **1**. ^{1}H NMR spectral analysis of the γ-lactone indicated that its gross structure was identical with that of the acid hydrolysis product from oscillatoxin A; its optical rotation, however, was opposite in sign with that of the degradation product [7], but matched that of the γ-lactone synthesized from (*S*)-(−)-malic acid [6, 7].

No debromoaplysiatoxin or oscillatoxin A-type compounds were found in the extract. The extract of this Puerto Rican *L. majuscula* showed no tumour promoting



1

activity; for example, the extract did not induce cell adhesion of human promyelocytic leukemia cells (HL-60) [8, 9].

EXPERIMENTAL

Isolation. Lyngbya majuscula was collected near the University of Puerto Rico Marine Station, Mayaguez, Puerto Rico in June, 1983. The freeze-dried alga (0.4 kg) was extracted twice with CH_2Cl_2–propan-2-ol (1:1) to give 2.2 g of extract. A portion of the extract (1.8 g) was subjected to gel filtration on Sephadex LH-20 (2.5 × 10 cm) using 400 ml of hexane–CH_2Cl_2 (1:4), 485 ml of CH_2Cl_2–Me_2CO (3:2), and 1.05 l. of CH_2Cl_2–Me_2CO (1:4). The fraction eluting at 735–1335 ml (43 mg) was then chromatographed on silica gel (2 × 2 cm) (TLC grade) using a hexane–EtOAc gradient. The 9 mg of oil which was eluted with hexane–EtOAc (1:1) was purified by HPLC on Partisil using CH_2Cl_2–EtOAc (4:1) to give (*S*)-(−)-3,4-dihydroxybutanoic acid γ-lactone (**1**) in 0.0015% yield: $[\alpha]_D - 80°$ ($CHCl_3$; *c* 0.5); EIMS *m/z* 102 $[M]^+$; ^1H NMR ($CDCl_3$): δ 4.69 (*m*, H-3), 4.41 (*dd*, $J = -10.2$ and 4.5 Hz, H-4 *trans* to OH on C-3), 4.29 (*dt*, $J = -10.2$ and 1 Hz, H-4 *cis* to OH on C-3), 2.75 (*dd*, $J = -18.0$ and 6.0 Hz, H-2 *trans* to OH on C-3), 2.52 (*dt*, $J = -18.0$, 2 and 1 Hz, H-2 *cis* to OH on C-3).

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