

琉球大学学術リポジトリ

Bioactive Metabolites from Okinawan Marine Organisms

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It has been amply demonstrated that marine organisms are prolific producers of novel bioactive metabolites. As part of our continuing chemical study of Okinawan marine organisms, we examined constituents of two soft corals (*Cespitularia* sp. and *Xenia* sp.). Alcyonolide (a xenicane diterpene) and its derivatives were isolated from the soft coral *Cespitularia* sp. whose ethyl acetate (EtOAc) extract displayed inhibition of the first cleavage of fertilized sea urchin eggs. The soft coral *Xenia* sp., of which crude EtOAc extract showed cytotoxicity against HCT116 (human colorectal cancer) cells, contained diterpene dialdehyde and its congeners. We will also report two diketopiperadines from an unidentified marine fungus.

We have so far isolated many C₁₁ compounds such as didemnenones and pentylphenols from ascidian *Lissoclinum* spp. and *Diplosoma* spp. Didemnenones and the related compounds have also isolated from cyanobacteria and sponges. Isolation of a series of the C₁₁ compounds from unrelated marine organisms supports the potential microbial origin of these compounds. From this viewpoint, it was assumed that ascidians might not be the real producer of these interesting compounds, but had any possible microorganism source such as a *Prochloron* sp. A *Prochloron* sp., is obligatory symbiont of ascidians, was separated from the body of an ascidian *Diplosoma* sp. by squeezing through plankton net and extracted with acetone. ¹H NMR of the crude extract showed the presence of the same peaks as present in the pure compound. Therefore, it was assumed that a *Prochloron* sp. was the real producer of the C₁₁ compounds. Most C₁₁ compounds are derived from polyketides, precursor **A** (six acetates) or precursor **B** (five acetates + C₁). Compounds which have a carbon skeleton of 5-methyldecane and pentylphenols are known to be derived from the precursor **A** with loss of CO₂. Compounds which have a carbon skeleton of 4-methyldecane are biosynthesized from precursor **B**. Since the didemnenone-related compounds have a common carbon skeleton of 4-methyldecane, we suggest that these compounds should be derived from the polyketide precursor **B**.

Synthesis of a new bromopentylphenol (a C₁₁ compound) was attempted, which showed ability to inhibit cell division of fertilized sea urchin eggs, because decomposition of this compound prevented us from characterizing it clearly. The synthesis of the bromopentylphenol was started with 2-bromo-5-methoxybenzoate (**1a**). The Grignard reaction of **1a** with pentylmagnesium chloride afforded alcohol **1b**. Mesylation of **1b** followed by reduction of the mesylate with NaBH₄ gave 4-bromo-3-pentylanisole (**1d**). Cleavage of the ether **1d** with phenyltrimethylsilane/iodine yielded the sole product. The product was identical to the naturally occurring compound.