沖縄産海洋生物の新規二次代謝産物の探索

Search for New Secondary Metabolites from Okinawan Marine Organisms

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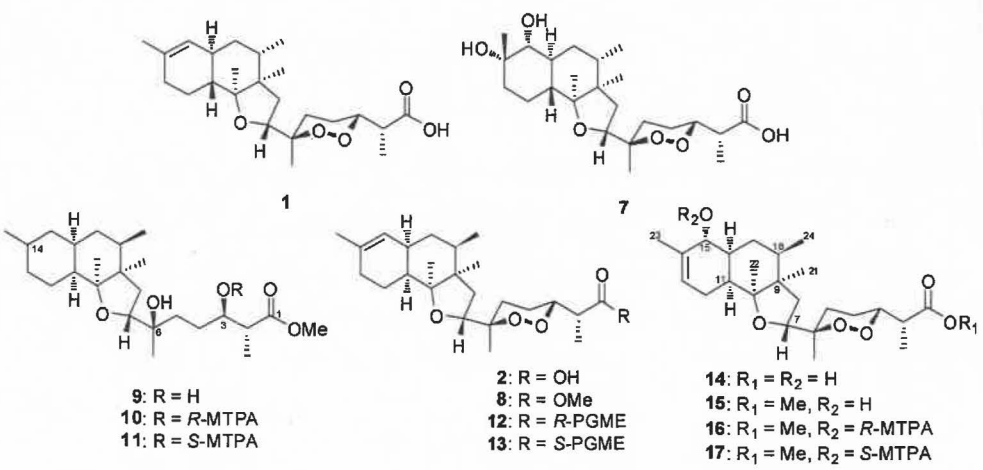
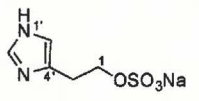
This dissertation is consisted of three independent projects: 1) chemical investigation on two new cytotoxic molecules from a sponge, 2) an imidazole derivative from another sponge, and 3) chemical and genetic variation of nudibranchs of Phyllidiidae.

After screening, two new norsesterterpenoids named trunculins X (**1**) and Y (**2**) were isolated from a sponge *Sigmosceptrella* sp. collected at Cape Hedo. With spectral data analyses, their structures were elucidated to be stereoisomers of trunculins, which had been reported from Australian sponges. The absolute configuration of trunculin X (**1**) was determined by X-ray crystallography of its diol derivative **7**, while that of trunculin Y (**2**) was solved by applying chiral derivatizing methods and spectroscopic analyses. The chirality at C-3 of **2** was solved by applying modified Mosher's method to compound **9** after methylation and hydrogenolysis of **2**. Stereochemistry of C-2 was determined by applying PGME method to **8**. An allyl alcohol **14**, obtained by mCPBA oxidation of **2**, was subjected for NOE study to elucidate stereochemistry of the tricyclic portion. In addition, modified Mosher's method was applied to C-15 of methyl ester **15** to determine the absolute configuration of **2**. Compounds **1** and **2** showed cytotoxicity against three cell lines: pancreatic carcinoma PANC-1, colon cancer HCT116 and rat bladder epithelial NBT-T2 at IC_{50} 0.32, 20 and 3.2 μM and at 0.39, 17 and 0.57 μM, respectively.



As a part of a collaborative project to find new antiviral compounds, an extract prepared from the black sponge *Dercitus* (*Halinastra*) *japonensis* was shown to inhibit human

immunodeficiency virus (HIV). After bioassay-guided separation, a new imidazole sulfate **18** and three known compounds **19–21** were characterized. The structure of compound **18** was elucidated by spectroscopic methods. One of the known compounds **19** showed weak anti-HIV activity at IC_{50} 109 μM.



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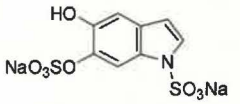
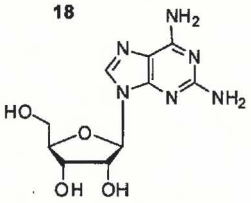
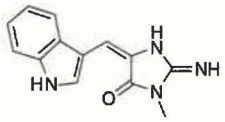


ancorinolate B (**19**)

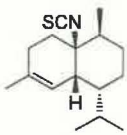


2-aminoadenosine (**20**)



2'-de-*N*-methylaplysinopsin (**21**)

On our interests on genetic and chemical diversity of the nudibranchs of the family Phyllidiidae, we collected a total of 154 specimens of nudibranchs and 16 specimens of prey sponges. All specimens were identified, and extracts prepared for examination of marker sesquiterpenoids. Two new iso(thio)cyanosesquiterpenoids **28** and **29** were isolated from a specimen of *Phyllidiella* sp.-1 collected at Cape Hedo. Their planar structures and relative configurations were elucidated by spectroscopic analyses and by comparison of the data with known compounds. The extracts were analyzed statistically for chemical diversity using ^{1}H NMR spectral data. Our collaborator also analyzed genetic diversity of the nudibranchs using COI (cytochrome oxidase I).



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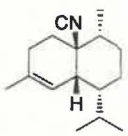

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To visualize the relationship between chemical constituents of the nudibranchs and their prey sponges, we applied principal component analysis (PCA) to ^{1}H NMR spectra of the extracts and of identified compounds with the software MestReNova. Then, we classified the extracts of nudibranchs and their prey sponges followed by linear discriminant analysis (LDA) of the spectral data. With the genetic analysis of the nudibranchs, we found that several clades of *Phyllidiella pustulosa* and close species contain a characteristic set of sesquiterpenoids suggesting the process of differentiation of nudibranchs.