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Marine Natural Products: Chemistry and Chemosystematics of the Gorgonian Genus *Eunicea* and Exploratory Studies of the Secondary Metabolites of Marine Fungi

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy in Oceanography

by

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ABSTRACT OF THE DISSERTATION

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Secondary metabolites of the Caribbean gorgonian genus *Eunicea* were extensively investigated through the systematic collection and assortment based on thin layer chromatographic (TLC) analysis. In addition, the chemical characters of *Eunicea* species were compared to the morphological classifications. In total, 792 individual

colonies were collected from four different locations of the West Indies. Based upon the TLC characters, 780 individual colonies were divided into 11 chemotypes. Seven chemotypes covered 8 of the 12 taxonomically defined species. Other four chemotypes possessed morphological features different from the known species and had potential to be classified as new species.

Detailed chemical investigation of 9 chemotypes resulted in the isolation of 39 new metabolites, along with 6 previously described compounds. Also, 3 compounds previously isolated from other organisms were also isolated in this work. Diterpenoids were the major group of metabolites, and cembranes were the most commonly encountered class. Other diterpenoids were dolabellanes, cubitanes, asperketals, fuscol and fuscol glycosides. Metabolites of three unprecedented classes were also isolated: C_{28} reduced quinones, trisnorditerpenoids and a diterpene glycoside of the "extended eremophilane" class. In addition to their structural determination, the irregular diterpenoid cubitanes were determined to be formed by a photochemically induced 1,3-acyl migration of a cembrane precursor.

Several chemotypes were collected from more than one location. Most chemotypes contained very distinct secondary metabolites. All of the studied chemotypes contained only one or two classes of metabolites. In the case where metabolites of a single class were isolated from more than one chemotype, there were great structural similarities among metabolites from the same chemotype. Metabolites from different chemotypes often showed very distinct patterns of functionalization.

Chemical characteristics of each chemotype were compared to the morphological classification. There was a clear difference in the chemical contents between the *Eunicea* subgenera, *Eunicea s.s.* (*sensu strictu*) and *Euniceopsis*. *Eunicea s.s.* was a chemically homogeneous group, and all of the isolated metabolites were cembrane lactones. In contrast, *Euniceopsis* showed species-specific distribution of metabolites. Comparison of

chemical contents revealed that for the chemosystematics of the *Eunicea*, types and distributions of functional groups were as important characters as the carbon skeletons of metabolites.

Eighty marine fungal strains were isolated from various habitats. Also, 41 obligate marine fungi were obtained from collaborating mycologists. The fungi were successfully cultivated in liquid media. The extracts of 38 fungi showed significant anti-microbial activities and/or cytotoxicity. Based upon the results of bioactivity tests, TLC analysis, and proton NMR spectroscopic analysis of the extracts, several strains were selected for chemical investigation.

From the mass culture of the deuteromycete *Asteromyces cruciatus*, gliovictin, a multi-functional diketopiperazine of the gliotoxin class was isolated. Also, several trichothecenes of the verrucarin and roridin classes were isolated from the culture of an unknown fungus. In addition, a few small-sized metabolites were isolated. The future of marine fungi for chemical investigation is discussed.