CHAPTER I

INTRODUCTION

During the last 30 years, organic chemists have intensively studied the chemistry of marine natural products. The reasons that introduce these researchers to be interested in this field are the differences between the marine environment and the terrestrial environment. Among these differences are

(i) the greater density of the sea water than that of air, which makes the existence and the chemical communication of the large floating communities of plants and animals,

(ii) reduced absorption of light permitting photosynthesis only in a narrow surface zone, and

(iii) the skeleton materials, which are protein-dominated rather than carbohydrate-dominated.

These properties provide the more complicated food chain in the marine environment than that in the terrestrial environment. The properties also result in an abundance of filter-feeding sessile organisms, such as sponges or ascidians, which become the excellent substrates for epibionts and symbionts. These communities are very rare in terrestrial ecosystem (Scheuer, 1990).

In early investigation, the researchers previously considered on toxins causing seafood poisoning. The well-known toxins were tetrodotoxin, the toxin from pufferfish, and saxitoxin, the toxin from the toxic dinoflagellates. Both toxins show highly potent and specific action in blocking the nerve membrane sodium channel, and become the useful tools in the study of neurophysiology and neuropharmacology (Narahashi, 1988). The interest increased since a lot of compounds from other marine organisms were found. Among these compounds, some showed interesting activities. These bioactive compounds were focused and evaluated their importances as research tools or medicines.

Some examples of bioactive constituents from marine natural products are

(i) didemnins, a group of cyclic depsipeptides isolated from a tunicate, *Tridemnum solidum*, which are immunosuppressive, antiviral, and antitumor (Rinehart *et al.*, 1990, a),

(ii) bryostatins, the antitumor macrolides from bryozoan, *Begula neritima* (Munro, Luibrand, and Blunt, 1987),

(iii) ecteinascidins, the cytotoxic tetrahydroisoquinolines from a tunicate, *Ecteinascidia turbinata* (Rinehart *et al.*, 1990, a), and

(iv) manoalide, an antiinflammatory non-steroidal sester-terpenoid found in a sponge, *Luffariella variabilis* (Mayer and Jacobs, 1988).

These constituents are in progress of study in their activities, particularly didemnin B which became the first marine natural product that entered phase II clinical trials (Munro *et al.*, 1987).

Among the marine organisms, sponges are one of the most interesting animals in which organic chemists have paid attentions. The sponges, belonging to the phylum Porifera, are the most primitive metazoa. They are sedentary and feed on their food by filtering the microplanktons from sea water passing through the small holes on their bodies (Brusca and Brusca, 1990). This characteristic behavior provides some notable results. First, the filtration of sea water makes sponges as great reservoirs collecting the metabolites from marine microorganisms. Their pore-bearing bodies also make sponges' colonies to become one kind of ecosystems. A large number of epibionts and symbionts such as bacteria or other microorganisms reside in a unique association with their hosts. So, unusual metabolites which were produced by the microorganisms can be found in sponges (Hirata and Uemura, 1986). Furthermore, the sponges themselves sometime produce certain toxic metabolites. These metabolites are utilized to defend the sponges from their predators as well as to compete with other organisms for their settling spaces (Paul, 1988).

A large number of compounds were isolated from sponges. Ireland *et al.* reported in 1988 that between 1977 and 1985, there were approximately 25 % of marine natural products isolated from the sponges. Among those metabolites, the largest class of compounds found in sponges was terpenoids. Nitrogenous compounds were also found in sponges including unusual alkaloids and rare isonitriles. Most of these compounds had

been determined their bioactivities. Ireland *et al.* also reported that up to 82 % of metabolites from sponges were antimicrobial.

In the investigation of Rinehart *et al.* in 1981, sponges' metabolites showed the best trends to be bioactive compounds. The extracts from sponges were antimicrobial against bacteria, yeasts, and fungi, as well as antiviral and cytotoxic. These extracts were also at the top of priority list of active constituents from the marine organisms in each bioactivity determination.

Thailand possesses coastline extending approximately 2,000 km in the Indo-Pacific region. These coastlines reside along the Andaman Sea and the east and west coast of the Gulf of Thailand (Surin Majchacheep, 1989). These long coastlines provide large area of territorial waters, and also provides a large number of marine lives. The marine flora and fauna of Thailand, especially the planktonic organisms, which are found in the Andaman Sea and in the Gulf of Thailand may differ from those of other areas of the world.

As discussed previously in this chapter, sponges can represent as the great reservoirs of the metabolites from marine microorganisms. Although they are in the same genus or species, the sponges collected from different locations may contain different kinds of constituents because of different environments and communities. So far, there are very few studies about the bioactive constituents from the Thai sponges. In this work, a Thai sponge of the genus *Reniera* which was collected from Si-Chang Island, Chonburi Province, was selected to investigate its bioactive constituents. The dichloromethane extract from this sponge showed significant antimicrobial, cytotoxic against tumor cell line, and ichthyotoxic activities. Therefore, the main objectives for this investigation are as followings:

(i) to isolate and purify the bioactive constituents from *Reniera* sp.,

(ii) to identify and elucidate the chemical structures of the isolated compounds, and

(iii) to propose the basic structure-activity relationship of the isolated compounds.