CHAPTER I

INTRODUCTION

Located in the tropical hemisphere, Thailand exhibits plant biodiversity and has many kinds of plants, which have strong potential for serving as therapeutic applications, especially herbs. The people use of medicinal plants has gradually been accepted as a treatment in primary health care system. People believe that herbal medicines pose less noxious side effects than synthetic drugs, have reasonable costs and easily availability. Nowadays, Thai medicinal plants are widely used among people and the demand for modern drugs that are mostly imported from abroad will hopefully be declined. Researchers have attempted to develop herbal medicines in order to make them safe and to implement them properly as therapeutic agents in the same way as modern drugs. Therefore, the study of chemical constituents of medicinal plants and their pharmacological activities including clinical trial was very important to achieve this goal.

Plao (genus Croton) is a herbal plant in Thailand. It belongs to the Euphorbiaceae family. Thai researchers have studied the chemical constituents and bioactivity of a variety of Plao, such as Plao Noi (*Croton sublyratus* Kurz.) leading to plaunotol which acts as an antipeptic ulcer [(1)]. Plao Ngoen (*Croton cascarilloide* Raeusch.) can also be used as an antifebrile [(2)], and Plao Yai (*Croton oblongifolius* Roxb.) which was known to be used in curing of many diseases.

Plao Yai belongs to the Euphorbiaceae family [(3)]. Its scientific name is *Croton oblongifolius* Roxb. Plao Yai is interesting Thai medicinal plants because all of its parts are useful. For the bark is used to inhibit chronic enlargements of livers and remittent fever. The leaves can be used as a remedy to liver compliments, the fruits

and seeds are a purgative and can be used to treat of snake bites. The heartwood is a remedy of faint and the roots are used to treat dysentery [4].

Recently, *Croton oblongifolius* Roxb. from various locations in Thailand have been investigated for their chemical constituents. It was found that the main components of each specimen were different. For instance, two new cembranoid compounds, namely crotocembraneic acid and neocrotocembraneic acid were discovered in Amphoe Vichienburi, Petchaboon province [5]. Four new labdane compounds including labda-7,12(E),14-diene, labda-7,12(E),14-triene-17-al, labda-7,12(E),14-triene-17-ol and labda-7,12(E),14-triene-17-oic acid were discovered in Amphoe Pranburi, Prachaubkhirikhan province [6,7]. Moreover, from Amphoe Muang, Udonthani province, two new labdane compounds were discovered including labda-7,13(Z)-diene-17,12-olide and labda-7,13(Z)-diene-17,12-olide-5-ol and two clerodane compounds namely (-)-20-benzyloxyhardwickiic acid and hardwickiic acid [8]. From Amphoe Muang, Uttaradit province, four compounds were discovered namely (-)-pimara-9(11),15-diene-19-oic acid, (-)-pimara-9(11),15-diene-19-ol, (2E,7E,11E)-1-Isopropyl-1,4-dihydroxy-4,8-dimethylcyclotetradeca-2,7,11-triene-12-carboxylic acid and methyl-15,16-epoxy-12-oxo-3,13(16),14-clerodatriene-20,19-olide-17-oate [9]. Furthermore, from Amphoe Wangsapung, Loei province, three new labdane compounds were discovered, namely 3-acetoxy-labda-8(17),12(E)-triene-2-ol, 2-acetoxy-labda-8(17),12(E)-triene-3-ol and labda-8(17),12(E)-triene-2,3-diol [10].

From the study of the cytotoxic activity of the chemical constituents of *Croton oblongifolius* Roxb. against P388 cells line and 6 tumor cell lines including HS27 (fibrobrast), Hep-G2(hepatoma), Chago (lung), SW620 (colon) Kato-3 (gastric) and BT 475 (breast), it has been reported that crotocembraneic acid and neocrotocembraneic acid show weak cytotoxic activity against the 6 tumor cell lines [5], labda-7,13(Z)-diene-17,12-olide-5-ol exhibit cytotoxic activity against the Hep-G2, Chago and Kato [8]. In addition, (-)-pimara-9(11),15-diene-19-ol shows moderate

cytotoxic activity against the Kato, Chago, SW620, Hep-G2 [9] and labda-8(17),12(E)-triene-2,3-diol are active with all cell lines, while 3-acetoxy-labda-8(17),12(E)-triene-2-ol is active with Kato and SW620, and 2-acetoxy-labda-8(17),12(E)-triene-3-ol is active with Kato and BT475 [10].

From the information above, *C. oblongifolius* Roxb. from different locations in Thailand give different diterpenoid compounds. The cytotoxicity test of the chemical constituents of *C. oblongifolius* Roxb. from different areas showed interesting results. The constituents may be useful of potential drugs. Thus, it is interesting to investigate the constituents and cytotoxicity activity of these plants from other locations in Thailand, which will give us a better understanding of the biodiversity and chemical diversity of this plant.

According to the $^{1}H.^{13}C$ NMR spectra of hexane crude extract from the stem barks of *C. oblongofolius* Roxb. from Amphoe Muang, Prachaubkhirikhan province, it was found to be different from $^{1}H,^{13}C$ NMR spectra of hexane crude extract from the stem barks of this plant found in other locations in Thailand. This implied that there were interesting compounds that are different from those obtained from other locations. Moreover, the stem barks of *C. oblongifolius* Roxb. in Amphoe Muang, Prachaubkhirikhan province have not yet studied. This thesis was emphasized on searching for the chemical constituents and biological activity of *C.oblongifolius* from this location.

The objectives of this research are summarized as follows:

1. To extract and isolate the diterpenoid compounds of the stem barks of *C. oblongifolius* Roxb. from Amphoe Muang, Prachaubkhirikhan province.
2. To elucidate the structure of the isolated substances.
3. To study cytotoxic activity of the isolated substances.