SUMMARY OF Ph.D. DISSERTATION

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Title

Chemical Studies on Biologically Active Tricyclic Compounds of Plant Origin

Abstract

Tricyclic compounds of plant origin are known to exhibit diverse biological activity, such as antibacterial, antitumor activity and enzyme inhibition. In this context, this thesis describes synthesis and biological evaluation of the following low-molecular weight natural products.

1. Chemical modification of mangostins

Mangostins carrying a xanthone core, which are rich components of *Garcinia mangostana* Lnn. (Guttiferae), have been reported to have a wide range of bioactivities such as antioxidative effect, antibacterial activity, and specific inhibition of acidic sphingomyelinase, although their cytotoxicity interfered with clinical use of mangostins. Previously prominent bioactivity of benzophenone-type congener of α-mangostin was observed in our laboratory. Accordingly, chemical modification of mangostin-class natural products will provide an access of assembly of new bioactive compounds. Along this line, their reactions under a variety of conditions have been attempted to obtain new derivatives possessing prominent biological activities, along with low cytotoxicities.

Among several derivatives examined, the γ-mangostin derivative, constructed by oxidation with an electrochemical method, was a potentaitor of the imipenem-activity against MRSA. In addition, *m*CPBA oxidation of α-mangostin provided a xanthone derivative possessing inhibitory activities on PDGF-mediated HASMC proliferation. Details of reaction pathway were also discussed.

2. Synthetic studies of megistophylline Ⅰ

Megistophylline Ⅰ, isolated from *Sarcomelicope megistophylla* Hartley (Rutaceae), is a tricyclic natural product carrying an acridone skeleton. This compound has a similar structural feature to that of γ-mangostin derivative, which was produced using electrochemical method. With the expectation of a similar bioactivity, a synthetic study of megistophylline Ⅰ was initiated.

The diarylamine precursor of the acridone was produced by the Ullmann protocol, and the following cyclization provided the expected tricyclic compound. Introduction of the appropriate substitution patterns was elabolated under such as anodic oxidation, and Claisen rearrangement conditions.