SUMMARY OF Ph.D. DISSERTATION

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Title

Synthetic studies on marine brominated natural products employing electroorganic chemistry

Abstract

Natural products, isolated as secondary metabolites of such marine origins as sponge, alga and sea hare, have served new and various structures with a variety of bioactivity. Since 1970, the phenyl pyruvic acid oxime derivatives containing spiroisoxazoline framework have widely been isolated as a main group of marine natural products containing halogen atoms. This family has potent bioactivities such as antimicrobial, antitumor, antifeedant activity, and so on. From the viewpoint of a variety of bioactivity, synthetic studies on spiroisoxazoline natural products have been started toward further bioactive evaluation. In this thesis, the following topics are described

1) Construction of spiroisoxazoline by electrochemical methodology.
Recently, electrochemical oxidation has increasingly progressed as a safety alternative to heavy metal or explosive oxidants in organic synthesis. Efficient construction of spiroisoxazoline was developed by anodic oxidation of the corresponding phenols.

2) Synthesis of aeroplysinins by new ring-opening access and their biological evaluation.
Efficient synthesis of aeroplysinins have been achieved by employing the ring-opening reaction through the N-O bond cleavage of spiroisoxazolines as a key step. Among them, several synthetic compounds showed a wide range of antimicrobial activity.

3) Synthesis, revised structure and biological evaluation of calafianin.
The reported structure of the natural calafianin and its isomer were successfully synthesized through the spiroisoxazoline compounds. Comparison of their spectroscopic data resulted in structural revision of the natural calafianin. In addition, a significant difference of their antimicrobial activities was observed.

4) Asymmetric synthesis of aerothionin employing optically active spiroisoxazoline derivative.
The successful first synthesis of optically pure (+)- and (–)-aerothionins from the racemic spiroisoxazoline derivative has been accomplished. The absolute configuration of natural (+)-aerothionin was determined by comparison of optically active spiroisoxazoline derivatives.

5) Synthetic studies on zamamistatin.
Zamamistatin, isolated from the Okinawan sponge, is a new member of the bromotyrosine derivative, and exhibited significant antibacterial activity against *Rhodospirillum salixigens*, possessing adhering properties. Accordingly, zamamistatin will be a valuable candidate for novel antifouling agents. In synthetic study, synthesis of dehydrozamamistatin has been achieved.