【Grant-in-Aid for Scientific Research (S)】

Science and Engineering (Chemistry)

Project Title : Studies on Chemical Synthesis of Polyketide-Derived, Biologically Active Complex Natural Products

Keisuke Suzuki
(Tokyo Institute of Technology, School of Science, Department of Chemistry, Professor)

Research Project Number : 16H06351 Researcher Number : 90162940
Research Area : organic chemistry
Keyword : natural products, polyketide, complexity, diversity, dimeric structure, hybridization

【Purpose and Background of the Research】

Even by the cutting-edge organic synthesis that provides now facile access to various useful compounds in scientific and industrial fields, certain classes of compounds remain inaccessible, due to the skeletal, functional, and stereochemical complexity. A typical example is the complex architectures derived from the type-II polyketide biosynthesis, constituting an attractive class of compounds with potential bioactivities. In this five-year project, we will address synthetic studies of such natural products by focusing on the development of new synthetic strategies and tactics, hoping eventually to achieve the total syntheses.

【Research Methods】

We sought a hint from natural biosynthesis and considered how the complexity and diversity of natural product structure evolved, recognizing three factors, 1) modification of the basic building unit **A** within itself, giving analogues $\mathbf{A_1}$, $\mathbf{A_2}$, $\mathbf{A_3}$…, 2) oligomerization, in particular dimerization, of **A**, and 3) hybridization with other biosynthetic constructs **B**, **C**, giving **A**–**B**–**C**. Centering attention to the type-II polyketide biosynthesis, intensive study will be carried out on the chemical synthesis of biologically active complex natural products.

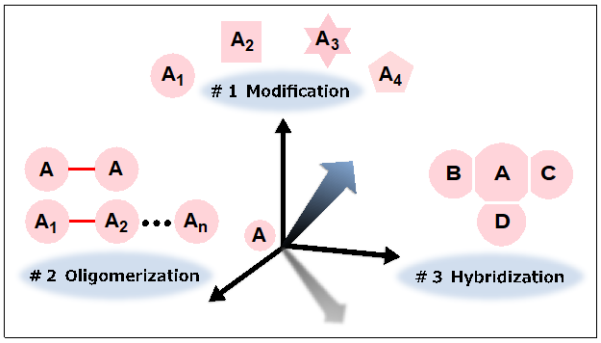

Fig.1 Structural diversity of natural products

【Expected Research Achievements and Scientific Significance】

This project will explore new synthetic strategies and tactics that will allow access to complex structures that are unavailable from natural source or through conventional organic synthetic methods.

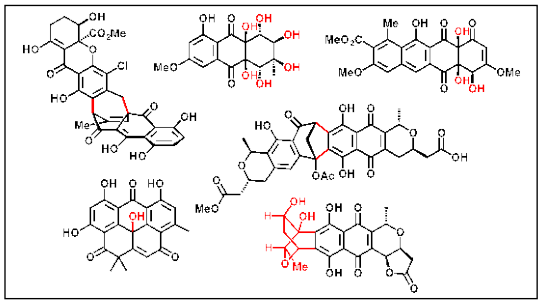

Fig 2. Selected synthetic targets

【Publications Relevant to the Project】

・"Total Synthesis of the Antibiotic BE-43472B", Y. Yamashita, Y. Hirano, A. Takada, H. Takikawa, K. Suzuki, *Angew. Chem. Int. Ed.* **2013**, *52*, 6658–6661.
・"Synthesis and Determination of the Absolute Configuration of Cavicularin by a Symmetrization/Asymmetrization Approach", H. Takiguchi, K. Ohmori, K. Suzuki, *Angew. Chem. Int. Ed.* **2013**, *52*, 10472–10476.
・"Synthesis of the Pluramycins 2: Total Synthesis and Structure Assignment of Saptomycin B, K. Kitamura, Y. Maezawa, Y. Ando, T. Matsumoto, K. Suzuki, *Angew. Chem. Int. Ed.* **2014**, *53*, 1262–1265.

【Term of Project】

FY2016-2020

【Budget Allocation】

141,800 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.chemistry.titech.ac.jp/~org_synth