Total Syntheses and New Biological Applications of Architecturally Complex Natural Products

Masayuki Inoue

(The University of Tokyo, Graduate School of Pharmaceutical Sciences, Professor)

【Outline of survey】

Natural products have been tremendously important in biology and human medicine because of their power to modulate signal transductions of biological system. Three-dimensional structures of natural products are highly optimized for function through evolutionary processes; functional information is manifested by sophisticated assemblages of various ring systems and functional groups. Since the removal of sub-structures of the natural products often leads to significant losses of their activity, total syntheses of their entire structures with a precision at an atomic level are necessary to provide sufficient amounts of material required for biological and medical applications. Architecturally complex natural products with molecular weight over 1000 are capable of highly specific interactions with their target proteins. Therefore, they are powerful agents for selectively controlling intricate biological systems. In this research, we will develop new and efficient synthetic methodologies and strategies for the synthesis of highly complex compounds. We will then apply the synthetic natural products and designed artificial analogs for studying new functions and network of biological systems.

【Expected results】

The goal of our research program is efficient, practical and flexible syntheses of biologically important natural molecules. At the core of this research program is the development of new strategies for assembling architecturally complex natural products in a concise fashion. These synthetic developments would enable unified synthesis of new artificial analogs by modification of natural products templates. The new synthetic methods for the natural products and the synthetic analogs will allow us to tailor and enhance their druglike properties, to gain control over diverse signal transductions thereby offering new research methods for the study of life science.

【References by the principal researcher】

- M. Inoue, M. Hirama, et al. “Total Synthesis of Ciguatoxin and 51-HydroxyCTX3C,” *J. Am. Chem. Soc.* **2006**, *128*, 9352-9354.
- M. Inoue et al. “Total Synthesis and Bioactivity of an Unnatural Enantiomer of Merrilactone A: Development of an Enantioselective Desymmetrization Strategy,” *J. Org. Chem.* **2007**, *72*, 3065-3075.

【Term of project】 FY2008－2012

【Budget allocation】
81,200,000 yen (direct cost)

【Homepage address】 http://www.f.u-tokyo.ac.jp/~inoue/e_index.html