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

Broad Section E

Title of Project： Practical synthesis of rare and structurally complex natural products and the development of the molecules with better biological functions

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【Purpose and Background of the Research】

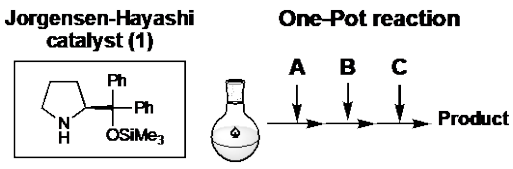
Natural products have a treasure trove of functions. Excellent medicines have been developed based on natural products. However, the science of rare natural products with complex backbones remains unexplored, because of their scarcity. If rare and biologically active natural products with complex skeletons can be synthesized in a short time with an enough quantity, they could open the door to a new science.

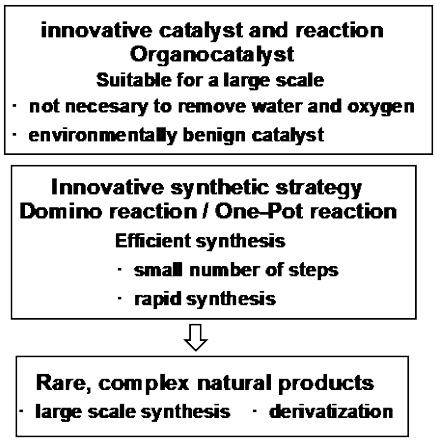
Efficient synthesis is one of the current trends in natural product synthesis, but it is a challenge to synthesize the complex natural products on a large scale. I have developed an innovative "Jorgensen-Hayashi catalyst (**1**)", and found many practical asymmetric reactions with excellent enantioselectivity. I also developed the new concept of pot economy, where multiple reactions are carried out in the same reaction vessel. Therefore, it would be possible to synthesize unexplored, rare natural products efficiently on a large scale by combining the organocatalyst mediated asymmetric reactions with pot economy. Moreover, if the synthetic method of the natural products can be accomplished, the creation of derivatives with better biological properties can be possible.

【Research Methods】

Organocatalysts are practical catalysts, because it is not necessary to remove water and oxygen from them completely, and there is no fear of metal contamination in the final compounds. Moreover, oragocatalysts are usually inexpensive. I have developed "Jorgensen-Hayashi catalyst **1**", which is an effective catalyst for many asymmetric reactions.

On the other hand, I proposed the concept of pot economy in the synthesis of molecules. One-pot operations serve as effective method for both carrying out several transformations and forming several bonds in a single-pot, while at the same time cutting out several purifications, minimizing chemical waste generation, and saving time.





Organic natural products with strong biological activity will be synthesized using the combination of organocatalyst and the concept of pot economy. Target molecules include amphotericin B, amphdinolide, prostaglandin, and steroids.

【Expected Research Achievements and Scientific Significance】

Natural products, which are difficult to obtain from natural sources and are difficult to synthesize because of their complex structure, can not to be investigated for their biological functions due to their scarcity. The practical synthesis of these natural products on a large scale will make a new science. Moreover, it can also provide derivatives with better biological functions.

【Publications Relevant to the Project】

・Pot economy and one-pot synthesis, Y. Hayashi, *Chem. Sci*., **2016**, *7*, 866-880.
・Time Economical Total Synthesis of (−)-Oseltamivir, Y. Hayashi, S. Ogasawara, *Org. Lett*., **2016**, *18*, 3426-3429.

【Term of Project】 FY2019-2023

【Budget Allocation】 133,300 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.ykbsc.chem.tohoku.ac.jp/