Department of Organic Chemistry

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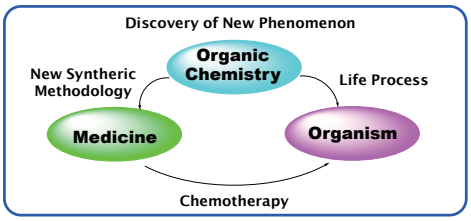
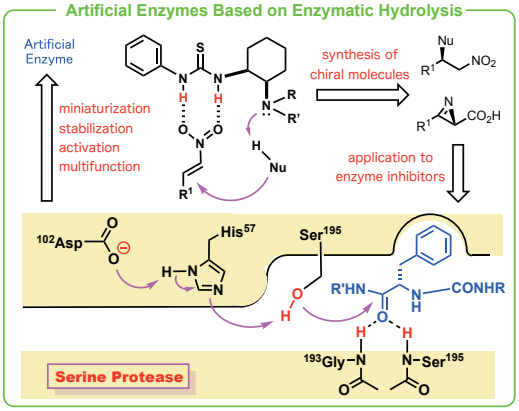
Research Projects:

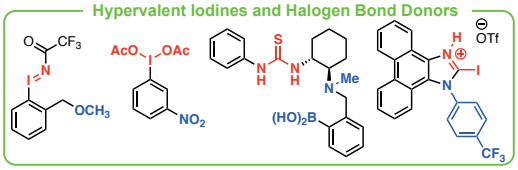
The aims of organic chemistry are structure analysis, reactivity studies, and the synthesis of organic molecules. The importance of organic chemistry in pharmaceutical sciences is clearly illustrated by the following facts: medicines are organic molecules that regulate life processes to cure diseases, and the targeted life processes are composed of organic reactions. With these properties in mind, our research programs are directed to the efficient construction of bioactive molecules and the development of new methodologies for the investigation of biological processes by utilizing these organic molecules.



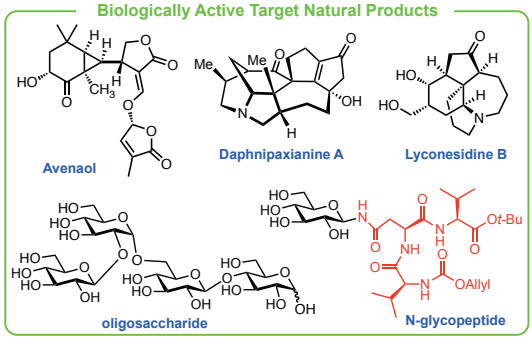
1) Development of Artificial Enzymes and Their Applications: Is it possible to create organic molecules capable of catalyzing reactions in place of enzymes? This was the starting point of our journey to the development of artificial enzymes, so-called organocatalysts. A close investigation of enzymes, such as serine protease, gave us an idea to design a small molecule, which possesses a hydrogen bonding site together with a basic amino group. After screening, a series of bifunctional thioureas were found to catalyze a wide range of stereoselective transformations. Asymmetric total syntheses using the thioureas have been achieved. We now have a broad catalyst library for a wide range of asymmetric reactions.



2) New Reagents and Catalysts for Glycopeptides: Chemical reactions without catalysts or promotors have great potential for the late-stage functionalization of bioactive compounds and prodrug synthesis. We designed *N*-acyliminoiodinanes activated by photoirradiation at 370 nm to allow a series of amination reactions with various electron-rich alkenes and alkynes. For example, the reaction with silyl enol ethers gave α-aminoketone derivatives in good yields. Furthermore, we found that α-ketoacids were converted to reactive acylating agents with hypervalent iodine(III) species, and established a novel decarboxylative acylation of amino acids and alcohols into peptides and esters without producing toxic wastes.



3) Total Synthesis of Natural Products: Natural products found in nature are expected to be the seeds of medicine in the future. We are engaged in the total synthesis of highly functionalized complex natural products in order to find the best way to rapidly synthesize an unprecedented structure. We thought that transition metals would have a key to finding an efficient solution. We have accomplished the total synthesis of avenaol using Rh and Ir catalysts. To challenge complex glycoproteins such as branched oligosaccharides and N-glycosyl peptides, new boron-hybrid catalysts and halogen bond donor catalysts have been developed. We aim to discover medicinal seeds by achieving rapid and gram-scale synthesis of valuable molecules.



Recent publications

- Hayama, N.; Kuramoto, R.; Földes, T.; Nishibayashi, K.; Kobayashi, Y.; Pápai, I.; Takemoto, Y. *J. Am. Chem. Soc.*, **2018**, 140 (38), 12216-12225.
- Nanjo, T.; Kato, N.; Takemoto, Y. *Org. Lett.*, **2018**, 20 (18), 5766-5769.
- Kobayashi, Y.; Nakatsuji, Y.; Li, S.; Tsuzuki, S.; Takemoto, Y. *Angew. Chem. Int. Ed.* **2018**, *57(14)*, 3646-3650.
- Kobayashi, Y.; Masakado, S.; Takemoto, Y. *Angew. Chem. Int. Ed.* **2018**, *57(3)*, 693-697.