# Division of Synthetic Chemistry
## – Synthetic Organic Chemistry –

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## Scope of Research

The research interests of this laboratory include the development of advanced molecular transformation, total synthesis of biologically active products, and molecular recognition. Programs are active in the following areas: 1) asymmetric alkylation of carbonyl compounds based on “memory of chirality”, 2) organocatalysis for fine organic syntheses, 3) synthesis of unusual amino acids and nitrogen heterocycles, 4) regioselective functionalization of carbohydrates, and 5) the structural and functional investigation of heterochiral oligomers.

### KEYWORDS

Site-Selective Functionalization
Molecular Recognition
Organocatalysis
Dynamic Chirality
Unusual Amino Acid

### Selected Publications


Kawabata, T.; Moriyama, K.; Kawakami, S.; Tsubaki, K., Powdered KOH in DMSO: An Efficient Base for Asymmetric Cyclization via Memory of Chirality at Ambient Temperature, *J. Am. Chem. Soc.*, **130,** 4153-4157 (2008).

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Yoshida, K.; Furuta, T.; Kawabata, T., Organocatalytic Chemoselective Monoacylation of 1, *n*-Linear Diol, *Angew. Chem. Int. Ed.*, **50,** 4888-4892 (2011).

Hamada, S.; Furuta, T.; Wada, Y.; Kawabata, T., Chemoselective Oxidation by Electronically Tuned Nitroxyl Radical Catalysts, *Angew. Chem. Int. Ed.*, **52,** 8093-8097 (2013).

Tomohara, K.; Yoshimura, T.; Hyakutake, R.; Yang, P.; Kawabata, T., Asymmetric α-Arylation of Amino Acid Derivatives by Clayden Rearrangement of Ester Enolates via Momory of Chirality, *J. Am. Chem. Soc.*, **135,** 13294-13297 (2013).

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Takeuchi, H.; Mishiro, K.; Ueda, Y.; Fujimori, Y.; Furuta, T.; Kawabata, T., Total Synthesis of Ellagitannins via Regioselective Sequential Functionalization of Unprotected Glucose, *Angew. Chem. Int. Ed.*, **54,** 6177-6180 (2015).

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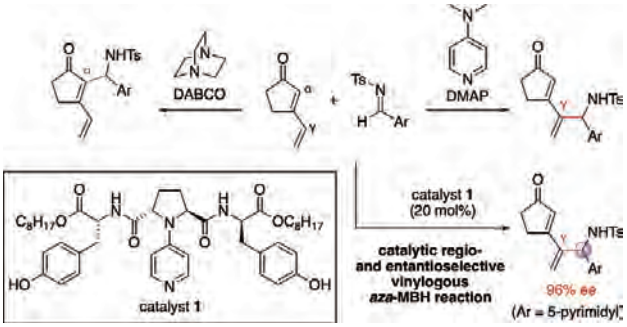
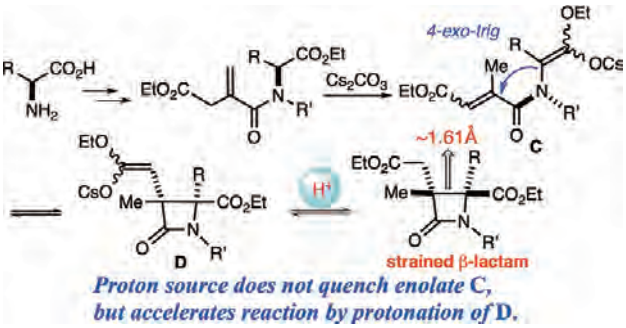
## Organocatalytic Regio- and Enantioselective Vinylogous *Aza*-Morita-Baylis-Hillman Reaction

The *aza*-Morita-Baylis-Hillman (*aza*-MBH) reaction is an effective carbon-carbon bond-forming reaction between electron deficient alkenes and aldimines to give the corresponding allylamines. For the construction of further densely functionalized molecules, an advanced version of *aza*-MBH reactions using conjugated dienes with electron-withdrawing groups has been studied. We have reported the first example of regiodivergent vinylogous *aza*-MBH reaction in a catalyst-controlled manner. Treatment of 3-vinylcyclopentenone with *N*-tosylaldimine and DABCO exclusively provided the α-adduct. In contrast, the corresponding reaction catalyzed by DMAP gave the γ-adduct selectively. Mechanistic analysis revealed that addition of proton sources accelerated the γ-selective reaction. Based on the findings, we designed original catalyst **1** possessing relatively acidic phenolic OH groups. Catalyst **1** successfully promoted enantioselective vinylogous *aza*-MBH reaction to afford the γ-adduct regioselectively in up to 96% ee.




## Asymmetric Synthesis of β-Lactams with Contiguous Tetrasubstituted Stereocenters from α-Amino Acids via Memory of Chirality

We have studied asymmetric reactions that proceed via enolate intermediates with dynamic chirality (memory of chirality: MOC). The major advantage of the strategy is the use of readily available α-amino acids as starting materials as well as the sole source of chirality. Since β-lactams still constitute one of the most important pharmacophores, and are useful as β-amino acid equivalents and chiral building blocks, development of synthetic methods for β-lactams is still of importance. Recently we developed a method for asymmetric synthesis of highly strained β-lactams with contiguous two tetrasubstituted stereocenters from readily available α-amino acids via a MOC strategy. In situ protonation of the labile β-lactam enolate intermediates formed through 4-*exo*-*trig* cyclization of the axially chiral enolates seems to be the key to successfully produce highly strained β-lactams. A salient feature of this transformation is that proton source does not quench the axially chiral enolate **C**, but accelerate the overall reaction by protonation of the intermediary β-lactam enolate **D**.




## Dirhodium-Catalyzed β-Selective C(sp$^3$)-H Amination of Organosilicon Compounds

Metal-catalyzed nitrogen-group-transfer via C-H bond cleavage has become an important tool for the construction of C-N bonds. While site-selective C-H functionalization has been extensively studied in intramolecular reactions, the development of intermolecular site-selective C-H functionalization is a further challenge in current organic synthesis. We recently found a dirhodium-catalyzed, intermolecular β-selective C-H amination of organosilicon compounds. Primary C(sp$^3$)-H bonds of silylethyl groups and secondary C(sp$^3$)-H bonds of silacycloalkanes can be selectively converted to C-N bonds at the β-position of the silicon atoms. The experimental data and theoretical calculations indicate that the strong σ-donor ability of the carbon-silicon bonds is responsible for the β-selectivity. Because silicon can be considered a bioisostere of carbon, the present protocol is applicable to synthesizing multi-functionalized organosilicon comounds with the potential to be powerful tools for drug discovery.