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

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Prof
KAWABATA, Takeo
(D Pharm Sc)

Assoc Prof
FURUTA, Takumi
(D Pharm Sc)

Assist Prof
UEDA, Yoshihiro
(D Pharm Sc)

Program-Specific Assist Prof
IMAYOSHI, Ayumi
(D Pharm Sc)

Techn Staff
FUJIHASHI, Akiko

PD
HARISADHAN, Ghosh
(Ph D)

PD
YELLA, Ramesh
(Ph D)

PD
CHANDA, Tanmoy
(Ph D)

PD
MORISAKI, Kazuhiro
(D Pharm Sc)

**Researcher (pt)**
HAYASHI, Kazuhiro

### Students

ARAI, Kenta (D3)
OTSUKI, Haruka (D3)
GONDOH, Naruhiro (D1)
SHIBAYAMA, Hiromitsu (D1)
MATAYOSHI, Aki (D1)
CHEN, Gong (D1)
XING, Yongning (D1)
SHIMMIYA, Ruri (M2)
NINOMIYA, Ryo (M2)
YAMAMOTO, Satoru (M2)
KUMEGAWA, Ryo (M2)
TAKASHIMA, Megumi (M2)
HASHIMOTO, Hisashi (M1)
FUJIMOTO, Takumi (M1)
MURAI, Takuya (M1)
WANG, Shuo (M1)
IKEDA, Ryohei (M1)
SUGA, Akihisa (M1)
TOMIGAHARA, Takayuki (UG)
WATANABE, Yuji (UG)

## 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**
Organocatalysis
Regioselective Functionalization
Dynamic Chirality
Unusual Amino Acid
Molecular Recognition

### 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).

Kawabata, T.; Jiang, C.; Hayashi, K.; Tsubaki, K.; Yoshimura, T.; Majumdar, S.; Sasamori, T.; Tokitoh, N., Axially Chiral Binaphthyl Surrogates with an Inner N-H-N Hydrogen Bond, *J. Am. Chem. Soc.*, **131,** 54-55 (2009).

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).

Yoshimura, T.; Tomohara, K.; Kawabata, T., Asymmetric Induction via Short-Lived Chiral Enolates with Chiral C-O Axis, *J. Am. Chem. Soc.*, **135,** 7102-7105 (2013).

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).

Ueda, Y.; Furuta, T.; Kawabata, T., Final-Stage Site-Selective Acylation for the Total Syntheses of Multifidosides A-C, *Angew. Chem. Int. Ed.*, **54,** 11966-11970 (2015).

## Catalyst-Controlled Site-Selective Asymmetric Epoxidation of Dienylamine Derivatives

Epoxidation is one of the most fundamental and important transformations in organic synthesis. While catalytic asymmetric epoxidation of allylic alcohols has been extensively developed, site-selective epoxidation of polyene compounds has been relatively unexplored. Here, we report the first example of highly site- and enantioselective expoxidation of dienylamine derivatives. Novel catalyst **1** has been developed for this purpose. Whereas *m*CPBA oxidation of a nerylamine derivative took place selectively at the more electron-rich double bond to give the 6,7-epoxides, catalyst **1** provides the 2,3-epoxides in high site- and enantioselectivity by the oxidation of relatively electron-deficient double bond: *Chem. Commun.* **2017**, *53*, 9320-9323**.** Themed Collections: Site-Selctive Molecular Transformation, Kawabata T. & Taylor M, Eds.

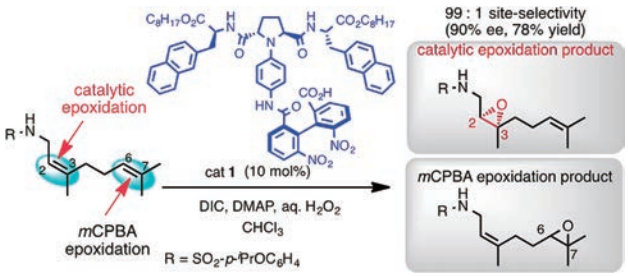


**Figure 1.**

## Organocatalytic Site-Selective Acylation of Carbohydrates with a Low Catalyst Loading by an In-Situ Counter-Anion Exchange Method

Site-selective catalysis has attracted increasing attention because of its potential utility for direct diversification of bioactive natural products and medicinal candidates with multiple functional groups. Especially, development of catalysts that can promote the target reaction in a site-selective manner independent from the intrinsic reactivity of the substrates, *i.e., catalyst-controlled selectivity*, is a challenging objective in current organic synthesis. We reported site-selective acylation of a glucose derivative with organocatalyst **2**. Acylation of the intrinsically less reactive C(4)–OH in the presence of the otherwise more reactive primary C(6)–OH proceeds via precise molecular recognition between the catalytic intermediate and the substrate. However, relatively high catalyst loading (1 mol %) was indispensable for this transformation. We report here a new catalytic system that enables the catalyst loading to be reduced to 0.01 mol %. Acylpyridinium ions such as **A** and **B** have been known as catalytically-active species in acylation reactions catalyzed by 4-dimethylaminopyridine and its analogues. Acylpyridinium carboxylates **B** were found to be 800–1300 times more reactive than the corresponding acylpyridinium chlorides **A**. This catalytic system in which acylpyridinium carboxylates were generated by *in-situ* counter anion-exchange from the acylpyridinium chlorides made possible to the catalyst loading as low as 0.01 mol % and catalyst turnover number of up to 6700 for site-selective acylation, retaining the high site-selectivity of acylation of the carbohydrate: *Org. Lett*. **2017**, *19*, 3099-3102.

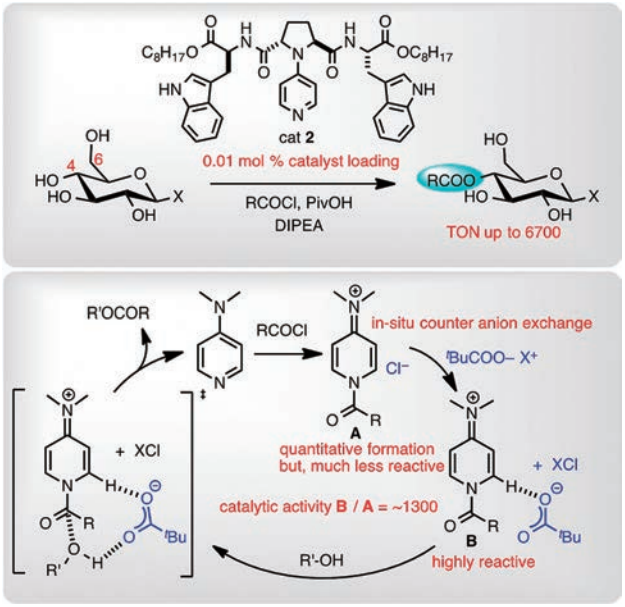


**Figure 2.**

## Asymmetric Desymmetrization of Aliphatic *meso*-Dial via Intramolecular Aldol Reaction Catalyzed by Aniline-type Acid Base Catalyst

Multiple-substituted cyclopentanes have attracted much attention as a core structure of pharmaceuticals as well as natural products. Asymmetric desymmetrization of aliphatic *meso*-1,6-dial through intramolecular aldol reaction provides one of the attractive ways for accessing functionalized cyclopentanes. We found that aniline-type acid base catalyst **3** discriminated the enantiotopic formyl groups of *meso*-dial and controlled four contiguous stereogenic centers well to give *anti-anti*-aldol adduct as a sole product in high diastereo- and enantioselectivities.

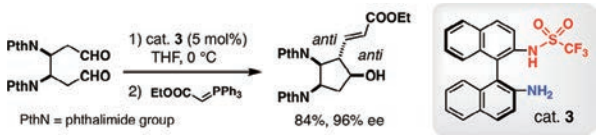


**Figure 3.**