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

Development of advanced molecular transformations based on innovative molecular design of higher order organosuperbase catalysts enabling molecular recognition

Principal Investigator	Tohoku University, Graduate School of Science, Professor TERADA Masahiro Researcher Number:50217428
Project Information	Project Number : 22H04969 Project Period (FY) : 2022-2026 Keywords : Asymmetric Synthesis, Organocatalyst, Hydrogen bonds, Organosuperbase, Catalyst

Purpose and Background of the Research

●Outline of the Research

Brønsted bases have been widely used as activators of reaction substrates with acidic protons, but they are now in the limelight because it has been revealed that organic molecules equipped with ultra-strong basicity exhibit specific reaction activity for molecular transformations that cannot be achieved with conventional organobases. In this study, we focus on higher order organosuperbase molecules, which have not been used as catalysts to date, and aim to develop their catalytic functions as well as to design and develop substrate-recognition-type higher order organosuperbase catalysts with substrate recognition capabilities, such as asymmetric recognition and molecular recognition. The ultimate goal is to develop higher order organosuperbase catalysts that realize high catalytic activity, straightforward molecular transformation, selective synthesis of chiral molecules, flexible control of stereochemistry, and recovery and reuse of catalysts based on innovative design concepts, and to develop unprecedented catalytic reaction systems, thereby bringing innovation to process chemistry in pharmaceutical and other fields.

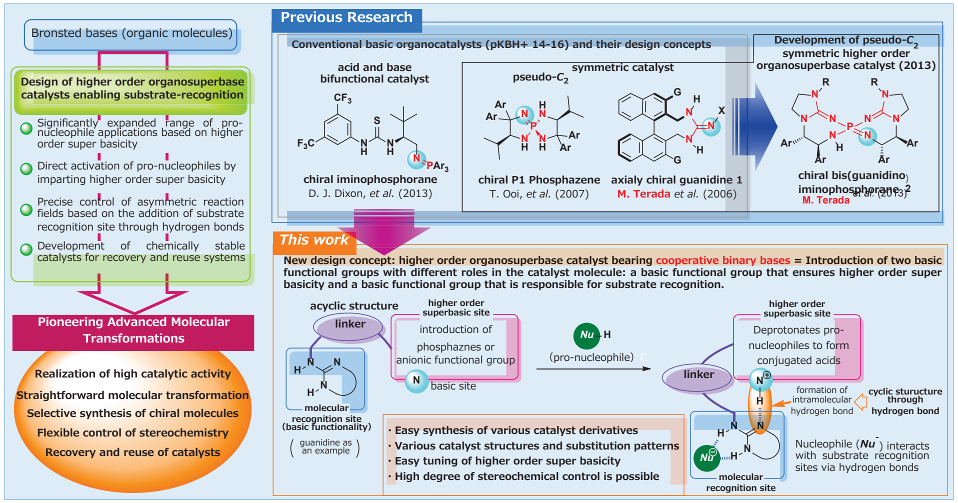

Figure 1. Molecular Design of Substrate Recognition-type and Higher Order Organosuperbases and Development of Catalytic Reaction Systems Using Them.

● Background and Purpose of Research

The development of advanced molecular transformations to reduce environmental impact has become one of the most important issues in synthetic organic chemistry. Brønsted bases have been widely used as activators of substrates with acidic protons, but in most cases, metal salts of organic molecules such as alkali metals and alkaline earth metals with strong basicity have been the mainstream. On the other hand, although organic bases are widely used as reactants in organic transformations, their basicity is not sufficient, limiting the target molecular transformations. In recent years, organic molecules with higher order super basicity have come into the limelight as they have been shown to exhibit unique reaction activity in molecular transformations that could not be achieved with conventional organic bases. However, molecular transformations using such strongly basic metal salts or higher order organosuperbases require the use of equimolar amounts, and little attention has been paid to the use of such salts or molecules as catalysts. This study focuses on Brønsted bases, especially higher order organosuperbases, which have not been used as catalysts to date, and aims to develop their catalytic functions as well as to design and develop substrate-recognition type higher order organosuperbases with substrate recognition capabilities such as chiral recognition and molecular recognition (Figure 1, left).

Expected Research Achievements

●What the research will achieve

It is not easy to design a catalyst molecule that incorporates such a super basic functional group into the catalyst molecule while providing a high level of substrate recognition ability. Based on the introduction of C_2 symmetry, which is the usual guideline for the design of asymmetric catalysts, we have succeeded in developing an axially chiral guanidine catalyst **1** and an organosuperbase catalyst **2** based on bis(guanidino)iminophosphorane core (Figure 1, upper right panel). However, when considering the development of various catalytic reaction systems, a fundamental reform of the catalyst design concept was inevitable. It is essential for the next generation of substrate-recognition type and higher order organosuperbase catalysts to realize "ease of synthesis of each catalyst derivative," "diversity of catalyst molecular structures and substitution patterns," and "ease of tuning of higher order super basicity," while overcoming the "addition of advanced stereochemical control ability. To solve these issues, we introduced an innovative design concept called "cooperative binary bases," and came up with the idea of developing substrate-recognition, higher order organosuperbase catalysts (Figure 1, lower right). This is a catalyst molecule design in which two basic functional groups with different roles, "a basic functional group ensuring higher order super basicity" and "a basic functional group responsible for substrate recognition," are introduced into the same molecule (Figure 2: Example **3**).

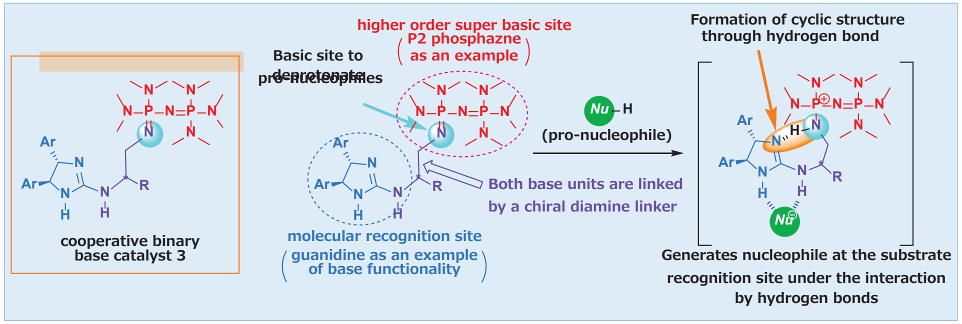

Figure 2. Higher order organosuperbase catalysts bearing cooperative binary bases.

Homepage Address, etc.	https://www.orgreact.sakura.ne.jp