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

Organic chemistry using water: development of aqua-organic chemistry

Principal Investigator	The University of Tokyo, Graduate School of Science, Professor KOBAYASHI Shu	Researcher Number:50195781
Project Information	Project Number : 22H04972 Keywords : synthetic organic chemistry, water, Lewis acid, base catalyst	Project Period (FY) : 2022-2026

Purpose and Background of the Research

●Background and Purpose of the Research

Chemistry plays an extremely important role in building a sustainable society. For example, fine chemicals such as pharmaceuticals, agrochemicals, and functional materials are indispensable to our daily lives, and organic chemistry has thus played a central role in their production. Modern organic chemistry has been cultivated based on the use of organic solvents. However, many organic solvents are harmful to the environment and the human body, and many are flammable and dangerous. In contrast to the long-standing belief that organic solvents are necessary for organic compounds to be reacted, one of the ideal chemical processes use water as a reaction medium. Can we build an organic chemistry using water instead of organic solvents? Our internationally acclaimed achievements in water-centered research would provide profound insights into the unique reactivities and selectivities found in organic chemistry explored exclusively in water. Continuous progress in this field is of crucial importance since cutting-edge research bolsters Japan's global competitiveness and status as a science-oriented nation. The applicant aims to make a paradigm shift from our reliance on organic solvents to water in order to achieve novel modes of chemical transformation.

●Outline of the Research

This project aims to develop catalysts that show high activity in water. Because organic compounds are not soluble in water, and many catalysts are deactivated by water, we need to tackle these problems. Desired catalysts provide high yields, high selectivities, and high turnover rates, in addition to recyclability, reusability, and broad applicability including asymmetric synthesis. In contrast, the "self-healing" without an external energy remains unattained. One of the main objectives of this research is to develop a self-healing catalyst that can work in water. There have been no examples of self-healing catalysts that can be used in asymmetric synthesis. In addition to the Lewis acid catalysts that have been developed so far, we will focus on Brønsted base catalysts that can work effectively in water to broaden the scope of new organic chemistry. We will also positively introduce other technologies such as organic electrochemistry.

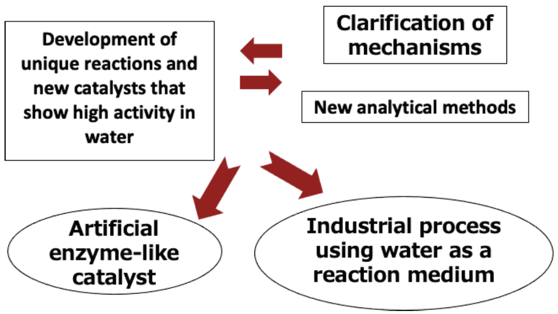

Figure 1. Outline of the Research

Clarification of mechanisms is also important. It is often difficult to apply existing analytical methods due to solubility issues. Therefore, we will also develop a new analytical method that can analyze heterogeneous catalytic reactions in water.

We will also aim at the actual production of fine chemicals such as pharmaceuticals, agrochemicals, and functional materials. To achieve this goal, we will study scaling up reactions using continuous-flow method. Catalyst developments are necessary for this purpose. We will also develop the work-up and purification techniques that do not use organic solvents. This study will also focus on recycling water.

Expected Research Achievements

●Five goals

In order to achieve the objective, the research will be conducted under the following five sub-themes: (1) development of highly active catalysts for efficient synthesis in water, (2) clarification of mechanisms in organic reactions developed in this study, (3) development of new methodology for analyzing organic reactions in water, (4) basic research for industrial processes using water as a reaction medium, and (5) construction of artificial enzyme-like systems in water.

(1) development of highly active catalysts for efficient synthesis in water

The development of new highly active catalysts in water is the most important in this research. For example, in addition to Lewis acid catalysts that have been studied for a long time, we will develop solid Brønsted base catalysts to broaden the scope of the new organic chemistry. We will expand the concept of a strong Brønsted base hybrid catalyst comprising a chiral bisoxazoline with an excess amount of a potassium base. We also found that metal oxides and hydroxides show unique catalytic activity in water. We'd like to combine these ideas. Another target is a self-healing catalyst. We will design and synthesize anion-containing ligands to provide a strong resistance to hydrolysis.

(2) clarification of mechanisms in organic reactions developed in this study

Since the interfaces formed between water, organics, and catalysts are conceived to play an important role in understanding the reactions performed in water, the reported organic reactions using water as a reaction medium are classified according to the interfaces. In order to further deepen understandings, we will elucidate the mechanistic differences of these reactions through spectroscopic and kinetic studies.

(3) development of new methodology for analyzing organic reactions in water

Due to the heterogeiety of the reaction solutions, common analytical methods such as NMR are difficult to use directly. To develop a new analytical method for heterogeneous catalytic reactions. Specifically, we will focus on mass spectrometry. The use of isotopically labeled indicator should allow quantitative analysis. We will use this method for many reactions developed in this research.

(4) basic research for industrial processes using water as a reaction medium

In the practical use, catalysts will be designed for continuous-flow methods instead of the batch method that has been traditionally used in organic synthesis. The continuous-flow method is superior because of its environmental friendliness, efficiency, and safety. Furthermore, we will study work-up and purification methods that do not use organic solvents. In addition, recycling water will be tested.

(5) construction of artificial enzyme-like systems in water

Because enzymes can perfectly control the stereoselectivity in water, artificially designed enzyme-like structure is a challenging task for organic chemists. We expect effective activation of both nucleophiles and electrophiles, efficient control of proton transfer by constructing the proper three-dimensional orchestration of Lewis acid/base, Brønsted acid/base, and hydrophobic moieties. Based on this concept, we will expand the scope of reactions.

Homepage Address, etc.	http://www.chem.s.u-tokyo.ac.jp/users/synorg/index.html Twitter: https://twitter.com/ShuKobayashiLab?ref_src=twsrc%5Etfw