Self-Assembling Molecular Systems Based on Coordination Chemistry

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1987 Ph.D. Tokyo Institute of Technology

Professional Employment
1982 Researcher, Sagami Chemical Research Center
1988 Assistant Professor to Associate Professor, Chiba University
1997 Associate Professor, Institute for Molecular Science
1999 Professor, Nagoya University
2002 Professor, The University of Tokyo
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Awards
1994 Progress Award in Synthetic Organic Chemistry, Japan
2000 Division Award of Chemical Society of Japan (Organic Chemistry)
2001 Tokyo Techno Forum 21 Gold Medal
2001 Japan IBM Award
2003 Nagoya Silver Medal
2004 Izatt-Christensen Award
2006 G. W. Wheland Award (Chicago University Lectureship Award)
2010 The Reona Esaki Award
2010 The JSCC Award
2011 3M Lectureship Award (University of British Columbia)
2012 Thomson Reuters Research Front Award 2012
2013 The Chemical Society of Japan (CSJ) Award
2013 Arthur C. Cope Scholar Award (ACS National Award)
2013 Merck-Karl Pfister Visiting Professorship (MIT Lectureship Award)
2014 ISNSCE 2014 Nanoprize
2014 Medal with Purple Ribbon
2014 Fred Basolo Medal (Northwestern University)
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2019 The Imperial Prize and the Japan Academy Prize
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We are designing new self-assembled molecular systems based on coordination chemistry, and apply the molecular system to various research fields. One of these examples is a molecular system called "crystalline sponge (CS)." The CS is a porous crystal, which can accommodate various kinds of small molecules, and align the accommodated molecules neatly in its inner space. Actually, we can observe the structure of the small molecules neatly aligned in the CS by the X-ray crystallography (Figure 1). Therefore, we can use the CS for the structure elucidation of the small molecules. This technique developed by us is called "CS method." The CS method has a potential to accelerate the various kinds of researches, in which the structure elucidation of novel compounds is required.

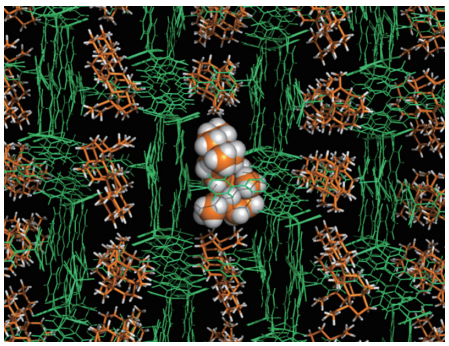

Figure 1. One example of the crystalline sponge method analysis result. Orange molecules are accommodated molecules, and green one is a framework of the crystalline sponge.

Selected Publications

- Y. Inokuma, S. Yoshioka, J. Ariyoshi, T. Arai, Y. Hitora, K. Takada, S. Matsunaga, K. Rissanen and M. Fujita, "X-Ray Analysis on the Nanogram to Microgram Scale Using Porous Complexes," *Nature* **495**, 461–466 (2013).
- D. Fujita, Y. Ueda, S. Sato, N. Mizuno, T. Kumasaka and M. Fujita, "Self-Assembly of Tetravalent Goldberg Polyhedra from 144 Small Components," *Nature* **540**, 563–566 (2016).

1. The CS Method Accelerates an Attempt to Create Artificial Natural Products

The natural products, compounds isolated from nature, exhibit great structural diversity and complexity. Such diversity and complexity of the natural products are generated by enzymatic reactions in organisms such as plants and bacteria. The enzymes can convert simple substrates into complex natural products. The natural products can be utilized for many kinds of purposes, such as medicines, industrial materials, and so on. Therefore, it can be said that the natural products are attractive resource for the exploration into useful compounds. However, recently, it becomes difficult to obtain new natural products with novel structures, because almost all types of natural products, which can be easily isolated, are considered to be already found through long history of natural product chemistry.

One way to solve this problem is a chemo-enzymatic approach. In this approach, we prepare unnatural synthetic substrates. Then, the substrates are converted into complex artificial molecules by enzymes, which is involved in the biosynthesis of natural products. In this way, we can expand the diversity of small molecules, using the biosynthetic mechanism of the natural products. One of the bottle-necks of this approach is the structural elucidation of the enzyme products, because the products often possess complex and unexpected structures. We consider that the CS method can solve this problem, since this method enables rapid structural elucidation of small molecules.

2. The CS Method Analysis of Artificial Indole-Containing Compound[1)]

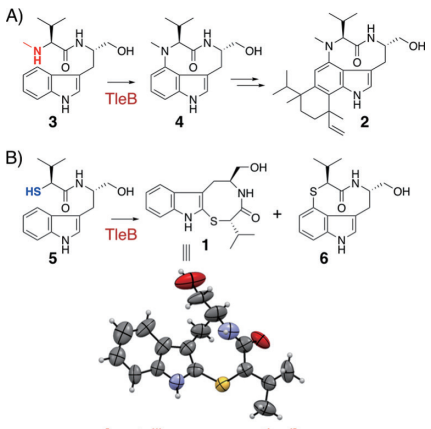

Figure 2. A) Reaction catalyzed by TleB in nature. B) Enzyme reaction to produce **1** and **6** from unnatural substrate **5**.

We elucidated a structure of a compound **1** generated by reaction using a biosynthetic enzyme, TleB, which is involved in a biosynthesis of **2** (Figure 2). In nature, TleB accepts **3** as a substrate and produce **4** (Figure 2A). However, it was found that unnatural substrate **5** could also be accepted by TleB, and **1** and **6** were generated (Figure 2B). Even though the structure elucidation of **6** could be accomplished by the NMR, MS, and single-crystal X-ray diffraction study, that of **1** could not be determined by the conventional methods. Therefore, we subjected **1** to the CS method, and succeeded in the structure elucidation.

3. The CS Method Analysis of Artificial Natural Products Produced by Enzymatic Cyclization Reaction[2)]

One of the important reactions to form basic skeletons of the natural products is a cyclization reaction. When a chemically synthesized unnatural substrate **7** was converted by an enzymatic cyclization reaction, **8** was generated (Figure 3). **8** has a novel structure, but its structure could not be determined by the NMR analysis. Thus, the structure of **8** was revealed by the CS method.

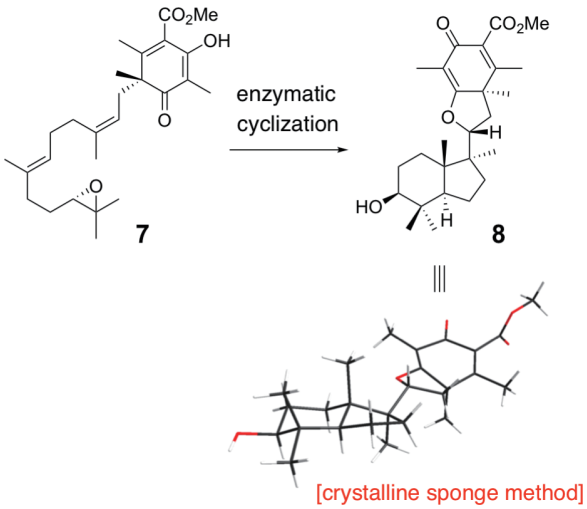

Figure 3. Enzyme reaction to produce **8** from **7**.

References

1) I. Morita, T. Mori, T. Mitsuhashi, S. Hoshino, Y. Taniguchi, T. Kikuchi, K. Nagae, N. Nasu, M. Fujita, T. Ohwada and I. Abe, *Angew. Chem., Int. Ed.* **59**, 3988–3993 (2020).

2) T. Mitsuhashi, L. Barra, Z. Powers, V. Kojasoy, A. Cheng, F. Yang, Y. Taniguchi, T. Kikuchi, M. Fujita, D. J. Tantillo, J. A. Porco and I. Abe, *Angew. Chem., Int. Ed.* **59**, in press (2020).

Award

FUJITA, Makoto; The 73rd Chunichi Cultural Award (2020).

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