Self-Assembling Molecular Systems Based on Coordination Chemistry

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Education
1980 B.S. Chiba University
1982 M.S. Chiba University
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
2018 Distinguished Professor, Institute for Molecular Science
2019 Distinguished Professor, The University of Tokyo

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)
2018 Wolf Prize in Chemistry
2019 The Imperial Prize and the Japan Academy Prize
2020 The 73rd Chunichi Cultural Award
2020 Clarivate Citation Laureates (Chemistry)
2020 "Major Results" of Nanotechnology Platform, MEXT
2022 Le Grand Prix 2022 de la Fondation de la Maison de la Chimie
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Our research is based on the design of new self-assembled molecular systems using coordination chemistry. We not only create the new self-assembled molecular systems but also research the application of them.

One example is a molecular system called crystalline sponge (CS). The CS is a porous crystal of a coordination network, into which various kinds of small molecules could be introduced. Notably, we can know structures of the small molecules accommodated in the pore of the CS by X-ray crystallography, because the accommodated small molecules periodically aligned in the CS. Thus, the CS can be utilized for the structure analysis, and this technique is called the CS method. This method has some advantages; i) only nanogram to microgram scale of analytes is required, ii) the absolute stereochemistry can be determined, iii) even oily substances can be analyzed by X-ray crystallography. Because of these fascinating features, the CS method attracts the interests of many people not only in academia but also in industry.

Besides structure analysis by the CS method, we also use the self-assembled molecular systems for various purpose, and try opening up new research field.

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).

Here, we show our recent progress. In the first case, we used the self-assembled molecular system for chemical reaction. In the second case, we applied the self-assembled molecular system to protein science.

1. Tetradehydro-Diels–Alder Reactions of Flexible Arylalkynes via Folding Inside the Self-Assembled Molecular Cage[1)]

The tetradehydro-Diels–Alder reaction is useful, but not so straightforward, requiring careful substrate design and harsh reaction consition. Recently, we found that efficient and site-selective tetradehydro-Diels–Alder reaction can be achieved by using a kind of self-assembled molecular system, called a Pd_6L_4 cage. The Pd_6L_4 cage has a cavity, into which broad range of compound can be introduced.

In the reaction we found, the substrate was captured inside the Pd_6L_4 cage, and the conformation of the substrate was fixed. The control of the substrate conformation results in the efficient and site-selective reaction (Figure 1).

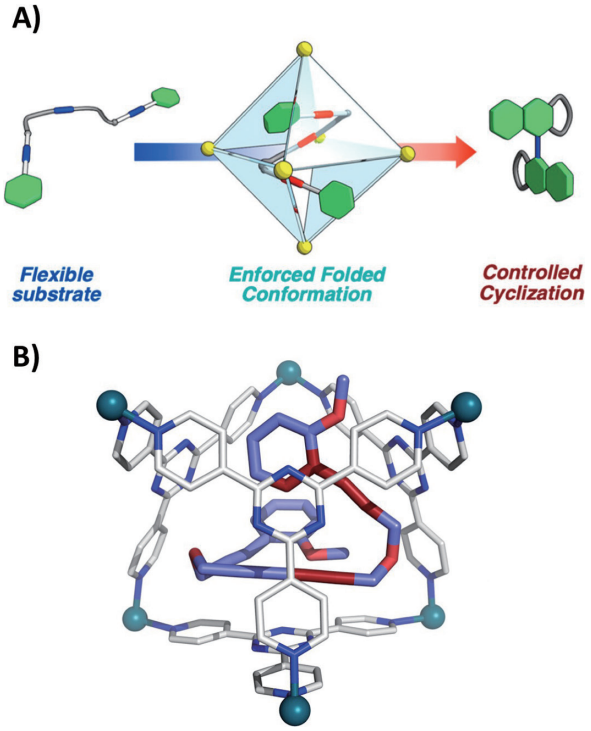

Figure 1. A) Concept of this study. B) Crystal structure of the substrate-Pd_6L_4 cage complex.

2. Hysteresis Behavior in the Unfolding/Refolding Processes of a Protein Trapped in the Self-Assembled Molecular Cage[2)]

The $M_{12}L_{24}$ self-assembled cage possesses a cavity large enough to accommodate proteins (Figure 2A).

Recently, we use this cage to analyze unfolding/refolding processes of a protein. When the concentration of organic solvent is increased in protein solution, the protein would be denatured. Then, the protein would be aggregated and precipitated normally. However, when the protein is captured in the self-assemble cage, the precipitation is prevented, because only single protein exists inside the cage. Thus, we can carry out the protein transient structure analysis, using this cage.

Concretely, we increase and decrease the concentration of acetonitrile of the protein solution, and the protein conformation was monitored by NMR analysis. As a result, it was revealed that the protein folding/unfolding process exhibited hysteresis behavior (Figure 2B).

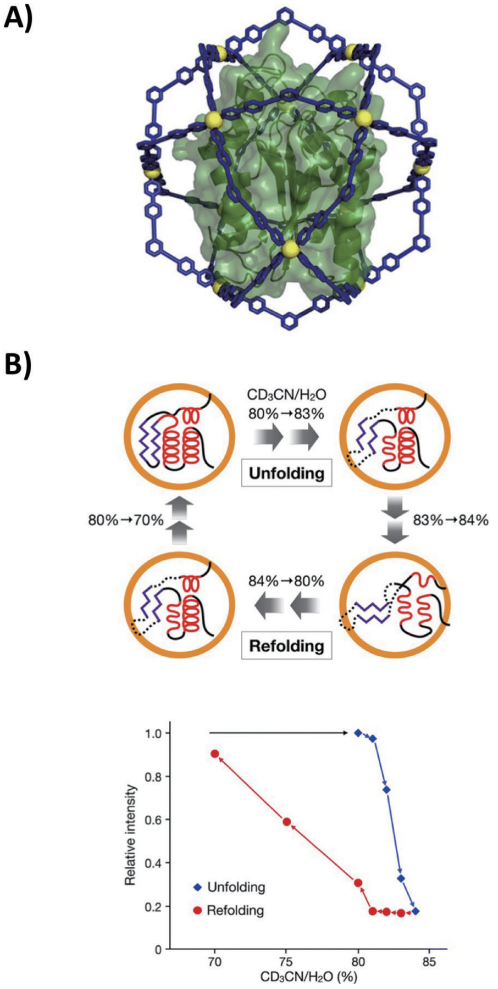

Figure 2. A) Molecular modeling of protein in the $M_{12}L_{24}$ self-assembled cage. B) Protein folding/unfolding process exhibited hysteresis behavior.

Award

FUJITA, Makoto; The Asahi Prize 2022 (2023).

References

1) G. R. Genov, H. Takezawa, H. Hayakawa and M. Fujita, *J. Am. Chem. Soc.* **145**, 17013–17017 (2023).

2) T. Nakama, A. Rossen, R. Ebihara, M. Yagi-Utsumi, D. Fujita, K. Kato, S. Sato and M. Fujita, *Chem. Sci.* **14**, 2910–2914 (2023).