RESEARCH ACTIVITIES

Division of Advanced Molecular Science

In this division, scientists of the first water are invited as “distinguished professors,” and the environment, in which they can devote themselves to their own research, is provided. The research in this division should be the last word in the field of molecular science.

Self-Assembling Molecular Systems Based on Coordination Chemistry

Division of Advanced Molecular Science

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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, Chiba University
1994 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

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

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Keywords Self-Assembly, Nano-Space, Coordination Chemistry

We are exploring new molecular materials with various three-dimensional architectures, utilizing the coordination chemistry. Especially, we are interested in materials, which possess inner space, because the inner space imparts new properties and functions to the materials. For example, we have developed a material called "crystalline sponge (CS)," which can accommodate many kinds of small molecules (Figure 1). Since the crystalline sponge can align the accommodated small molecules neatly in its inner space, we can carry out the structural elucidation of the accommodated molecules by the X-ray crystallography. This new structural elucidation technique is designated as "CS method," and attracting broad interests, because this method enables the X-ray analysis without the crystallization of target molecules.

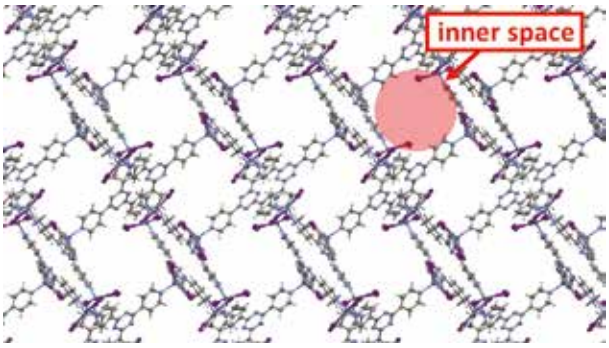

Figure 1. Network structure of the CS. There is inner space, into which various kinds of molecules could be introduced.

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. Structural Elucidation of a Novel Natural Product, Tenebrathin, by the CS Method[1)]

The natural product chemistry is one of the best fields, in which the CS method could be efficiently utilized. One of the goals of the natural product chemistry is an identification of new compounds with novel structures from nature. However, structures of natural products are, in many cases, very complex and hard to solve. But, if we use the CS method, we can easily and quickly observe the 3D-structure of target compounds. Thus, the CS method have a great potential to accelerate the study in the field of natural product chemistry.

To search for novel natural products, we investigated into metabolite of bacterium *Streptoalloteichus tenebrarius* NBRC 16177, and found a new compound, which we designated as tenebrathin (**1**). Firstly, the structure of **1** was investigated by the NMR (Nuclear Magnetic Resonance) analysis, and a partial structure of **1** could be solved. However, we could not know its complete structure. Actually, even though NMR is really strong approach to solve the structures of small molecules, NMR analysis is not a universal method. Sometimes, we encounter compounds, whose structures could not be solved by the NMR analysis. Moreover, the NMR analysis normally could not determine an absolute configuration. Thus, we subjected **1** to the CS method. As a result, the structure and the absolute configuration of **1** was clearly solved (Figure 2). These results have been obtained through a collaborative research with Prof. Ikuro Abe (the University of Tokyo, Japan).

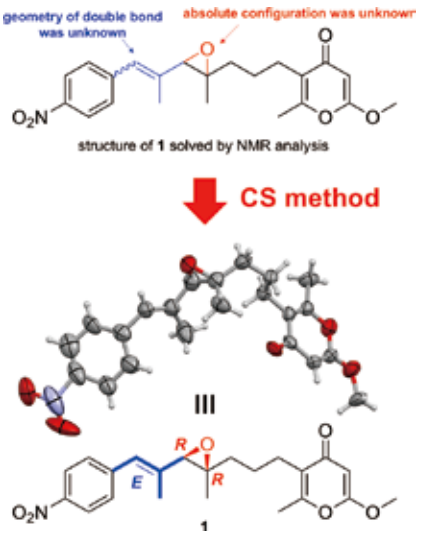

Figure 2. The chemical structure of **1**, and a crystal structure of **1**, which was observed by the CS method.

2. Structural Elucidation of a Biosynthetic Intermediate of Diosgenin[2)]

Diosgenin is a spiroketal steroidal natural product and one of the important compounds for the world steroid hormone industry, because diosgenin can be used as precursor of drugs. However, the biosynthetic pathway of diosgenin was unknown, and almost all diosgenin used in the industry are extracted from plant.

If we can solve the biosynthetic route of diosgenin, we would be able to pave the way for developing fermentative production process, which does not require the plant body to obtain diosgenin. Therefore, we tried to solve the biosynthetic pathway of diosgenin.

As a result, we identified enzymes responsible for the biosynthesis of diosgenin. At the same time, we also obtained compound **2**, a biosynthetic intermediate of diosgenin. However, only 1.5 mg of **2** could be obtained, and it was hard to determine its chemical structure only by the NMR and MS analysis. Therefore, we apply the CS method, and successfully elucidated the structure of **2** (Figure 3). These results have been obtained through a collaborative research with Prof. Jing-Ke Weng (Massachusetts Institute of Technology, USA).

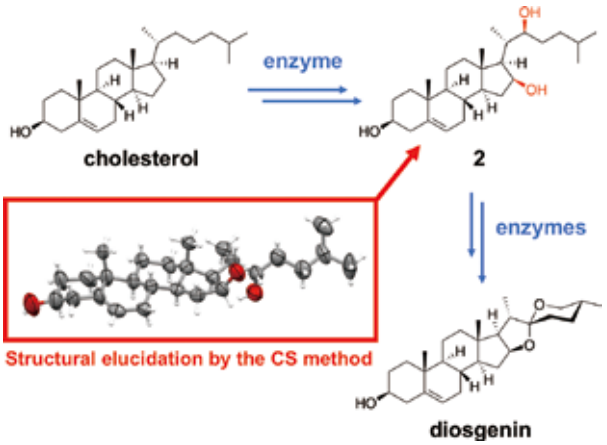

Figure 3. The biosynthetic pathway of diosgenin, and a crystal structure of **2**, which was observed by the CS method.

References

1) S. Hoshino, T. Mitsuhashi, T. Kikuchi, C. P. Wong, H. Morita, T. Awakawa, M. Fujita and I. Abe, *Org. Lett.* **21**, 6519–6522 (2019).
2) B. Christ, C. Xu, M. Xu, F.-S. Li, N. Wada, A. J. Mitchell, X.-L. Han, M.-L. Wen, M. Fujita and J.-K. Weng, *Nat. Commun.* **10**, 3206 (2019).

Award

FUJITA, Makoto; The Imperial Prize and the Japan Academy Prize (2019).

* carrying out graduate research on Cooperative Education Program of IMS with the University of Tokyo