

RESEARCH ACTIVITIES

Division of Advanced Molecular Science

The division consists of two sections. In the first one, 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 section should be the last word in the field of molecular science.

In the second section, we invite researchers in the universities performing unique researches in the field of molecular science as cross-appointment faculty members, and provide the research environment to enable research activity with advanced facilities in IMS.

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 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

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Secretary

MASUDA, Michiko

Keywords

Self-Assembly, Nano-Space, Coordination Chemistry

We are designing new self-assembled molecular systems based on coordination chemistry, and trying to apply the molecular system to various research fields.

For example, we applied the self-assembled molecular systems to biological studies and the structure elucidation of small molecules (Figures 1 and 2).

Currently, we are focusing on the following two projects:

(1) Protein encapsulation in self-assembled Coordination cages: In this project, we aim to explore the potential of proteins encapsulated within precisely designed molecular capsules (Figure 1). We envision to 1) control the property of protein (*e.g.*, stability, ligand affinity or selectivity), 2) control enzymatic reactivity (*e.g.*, activity or new function), and 3) develop new analytical methodology (coupled with NMR, X-ray, MS or cryoEM *etc.*).

(2) Crystalline sponge (CS) method: 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 2). The method has a potential to accelerate the various kinds of researches, in which the structure elucidation of novel compounds is required. We target to develop new drug discovery using this method.

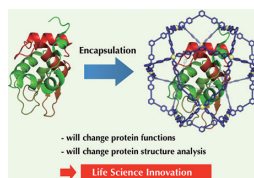


Figure 1. Cartoon presentation for the protein encapsulation.

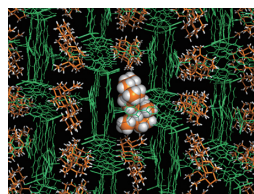


Figure 2. One example of the crystalline sponge method.

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. Protein Stabilization and Refolding in a Gigantic Self-Assembled Cage

Spatial isolation of molecules is often a powerful strategy for regulating their molecular behavior. Biological systems employ such mechanisms well; however, scientists have yet to rival nature, particularly for macromolecular substrates. We demonstrated that the encapsulation of a protein in a molecular cage with an open framework stabilizes the tertiary structure of the protein and improves its enzymatic activity. Particularly, when the three-dimensionally confined enzyme was exposed to an organic solvent, its half-life was prolonged 1,000-fold. Kinetic and spectroscopic analysis of the enzymatic reaction revealed that the key to this stability is the isolated space; this is reminiscent of chaperonins, which use their large internal cavities to assist the folding of client proteins (Figure 3). The single-molecule protein caging affords a new type of protein-based nanobiotechnology that accelerates molecular biology research as well as industrial applications.

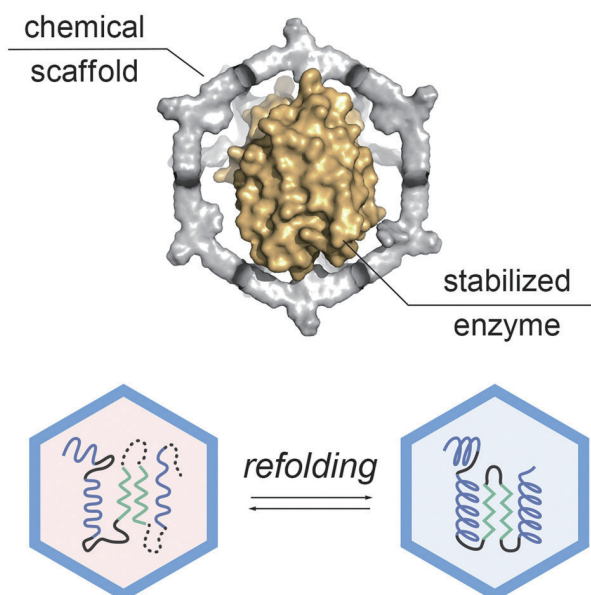


Figure 3. Protein refolding in the cage.

2. Absolute Configuration Determination from Low *ee* Compounds by the Crystalline Sponge Method

When chiral compounds with low enantiomeric excess (*ee*, $R:S = m:n$) were absorbed into the void of the CS, enantiomerically pure $[(R)_m(S)_n]$ chiral composites were formed,

Awards

FUJITA, Makoto; Clarivate Citation Laureates (Chemistry) (2020).

MITSUHASHI, Takaaki; FUJITA, Makoto; “Major Results” of Nanotechnology Platform, MEXT (2020).

changing the centrosymmetric space group into non-centrosymmetric one (Figure 4). The absolute configuration of the analyte compounds was elucidated with a reasonable Flack (Parsons) parameter value. This phenomenon is characteristic to the “post-crystallization” in the pre-determined CS crystalline lattice, seldom found in common crystallization where the crystalline lattice is defined by an analyte itself. The results highlight the potential of the CS method for absolute configuration determination of low *ee* samples, an often encountered situation in asymmetric synthesis studies, which is important for the development of new drugs.

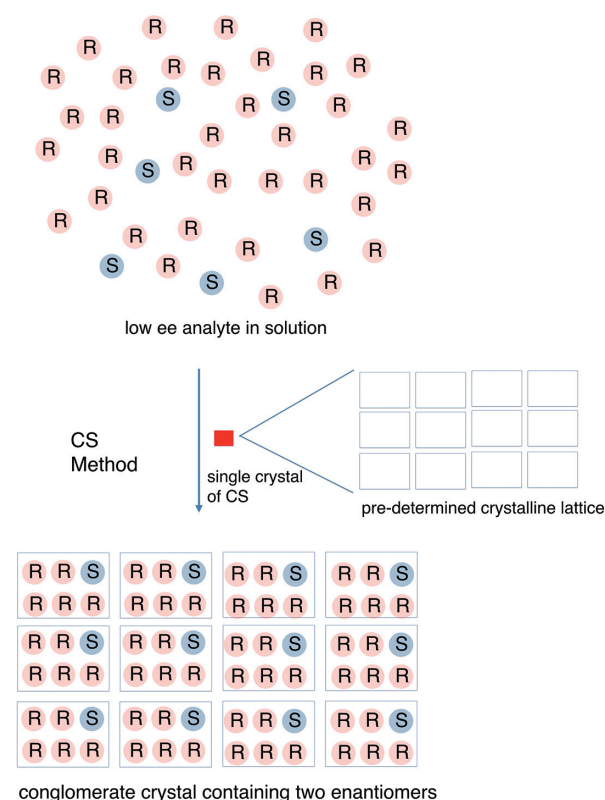


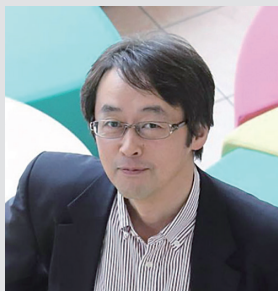
Figure 4. CS method was applied to the analysis of chiral compounds with low enantiomeric excess.

References

- 1) D. Fujita, R. Suzuki, Y. Fujii, M. Yamada, T. Nakama, A. Matsugami, F. Hayashi, J.-K. Weng, M. Yagi-Utsumi and M. Fujita, *Chem* **7**, (2021), in press.
- 2) R. Dubey, K. Yan, T. Kikuchi, S. Sairenji, A. Rossen, S. S. Goh, B. L. Feringa and M. Fujita, *Angew. Chem., Int. Ed.* **60**, 11809–11813 (2021).

Exploring Novel Physical Properties by Multi-Dimensional Spectroscopy

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Education

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Professional Employment

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1993 Research Associate, Kobe University
1993 Research Associate, Institute for Molecular Science
1998 Associate Professor, Kobe University
2002 Associate Professor, Institute for Molecular Science
2013 Professor, Osaka University
2020 Professor (Cross Appointment), Institute for Molecular Science

Awards

2001 Young Incentive Award, Japanese Society for Synchrotron Radiation Research
2008 The Commendation for Science and Technology by MEXT, Japan Science and Technology Prize (Research Field)
2008 Morita Memorial Prize

Member
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Keywords

Condensed Matter, Optical and Photoelectrical Properties, Synchrotron Radiation

Physical and chemical properties of solids, such as conductivity, magnetism, superconductivity and chemical reactions originate from microscopic electronic structure, lattice/molecular vibrations, and molecular movements based on quantum mechanics in materials and their interactions. By revealing the microscopic states, we can learn about the origin of physical and chemical properties and hidden functionalities. Also, the microscopic information is helpful for the creation of novel functional properties. To visualize hidden microscopic information, we develop novel spectroscopic techniques using synchrotron radiation, high brilliant electron beams, and other so-called quantum beams. We are now developing a new electron spectroscopy technique, namely Spin-Resolved resonant Electron-Energy-Loss Spectroscopy (SR-rEELS), with bulk-sensitive primary energies of 0.3–1.5 keV, as shown in Figure 1, in order to detect spin-selective element-specific bulk plasmons. Based on the obtained information of electronic structures, we aim to develop novel physical properties of new materials.

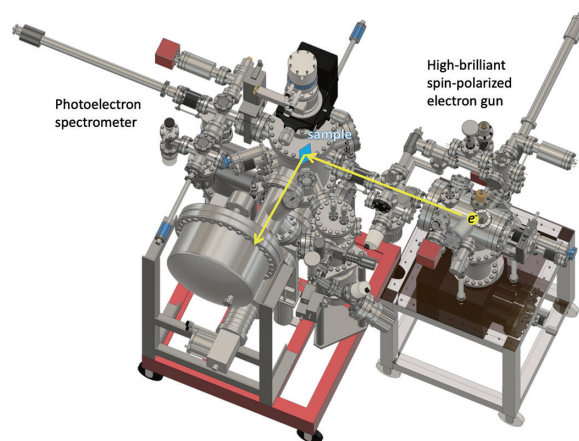


Figure 1. Spin-Resolved resonant Electron-Energy-Loss Spectroscopy (SR-rEELS) apparatus developed by our group. The apparatus consists of a high-brilliant spin-polarized electron gun and a photoelectron spectrometer.

Selected Publications

- Y. Ohtsubo, Y. Yamashita, K. Hagiwara, S. Ideta, K. Tanaka, R. Yukawa, K. Horiba, H. Kumigashira, K. Miyamoto, T. Okuda, W. Hirano, F. Iga and S. Kimura, "Non-Trivial Surface States of Samarium Hexaboride at the (111) Surface," *Nat. Commun.* **10**, 2298 (7 pages) (2019).
- K. Hagiwara, Y. Ohtsubo, M. Matsunami, S. Ideta, K. Tanaka, H. Miyazaki, J. E. Rault, P. Le Fèvre, F. Bertran, A. Taleb-Ibrahimi, R. Yukawa, M. Kobayashi, K. Horiba, H. Kumigashira, K. Sumida, T. Okuda, F. Iga and S. Kimura, "Surface Kondo Effect and Non-Trivial Metallic State of the Kondo Insulator YbB₁₂," *Nat. Commun.* **7**, 12690 (7 pages) (2016).
- S. Kimura and H. Okamura, "Infrared and Terahertz Spectroscopy of Strongly Correlated Electron Systems under Extreme Conditions," *J. Phys. Soc. Jpn.* **82**, 021004 (28 pages) (2013). [review]
- S. Kimura, T. Iizuka, H. Miyazaki, A. Irizawa, Y. Muro and T. Takabatake, "Electronic-Structure-Driven Magnetic Ordering in a Kondo Semiconductor CeOs₂Al₁₀," *Phys. Rev. Lett.* **106**, 056404 (4 pages) (2011).

1. Magneto-Optics of the Weyl Semimetal TaAs in the THz and IR Regions¹⁾

The magnetic-field dependence of optical conductivity [$\sigma(\omega)$] spectra of the ideal type-I Weyl semimetal TaAs has been investigated at the temperature of 10 K in the terahertz (THz) and infrared (IR) regions. The obtained $\sigma(\omega)$ spectrum in the THz region of $\hbar\omega \leq 15$ meV is strongly affected by the applied magnetic field (B): The Drude spectral weight is rapidly suppressed, and an energy gap originating from the optical transition in the lowest Landau levels appears with a gap size that increases in proportion to \sqrt{B} , which suggests linear band dispersions. The obtained THz $\sigma(\omega)$ spectra could be scaled not only in the energy scale by \sqrt{B} but also in the intensity by $1/\sqrt{B}$ as shown in Figure 2, which has been predicted theoretically. In the IR region for $\hbar\omega \geq 17$ meV, on the other hand, the observed $R(\omega)$ peaks originating from the optical transitions in higher Landau levels are proportional to linear- B suggesting parabolic bands. The different band dispersions suggests that the Dirac linear bands transition to the free-electron-like parabolic bands with increasing energy.

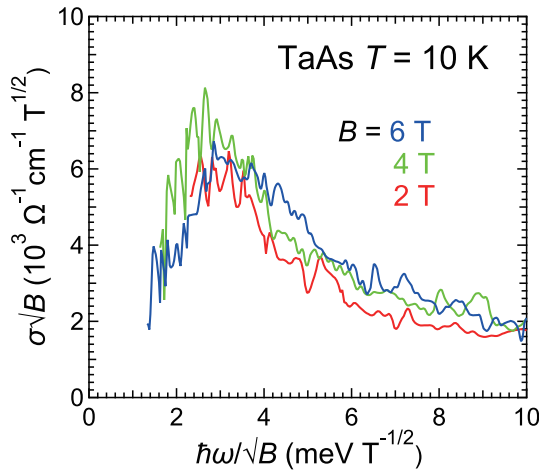


Figure 2. Magnetic-field dependence of optical conductivity [$\sigma(\omega, B)$] spectrum of TaAs in the THz region at the temperature of 10 K. The horizontal and vertical axes are normalized by B and $1/\sqrt{B}$, respectively.

2. One-Dimensionality of the Spin-Polarized Surface Conduction and Valence Bands of Quasi-One-Dimensional Bi Chains on GaSb(110)-(2×1)²⁾

Surface electronic structure and its one-dimensionality above and below the Fermi level (E_F) are surveyed on the Bi/GaSb(110)-(2×1) surface hosting quasi-one-dimensional (Q1D) Bi chains, using conventional (one-photon) and two-photon angle-resolved photoelectron spectroscopy (ARPES) and theoretical calculations. ARPES results reveal that the Q1D electronic states are within the projected bulk band gap. Circular dichroism of two-photon ARPES and density-functional-theory calculation indicate clear spin and orbital polarization of the surface states consistent with the giant sizes of

Rashba-type spin-orbit interaction (SOI), derived from the strong contribution of heavy Bi atoms. The surface conduction band above E_F forms a nearly straight constant-energy contour (Figure 3a), suggesting its suitability for application in further studies of one-dimensional electronic systems with strong SOI. A tight-binding model calculation based on the obtained surface electronic structure successfully reproduces the surface band dispersions (Figures 3b, 3c) and predicts possible one- to two-dimensional crossover in the temperature range of 60–100 K.

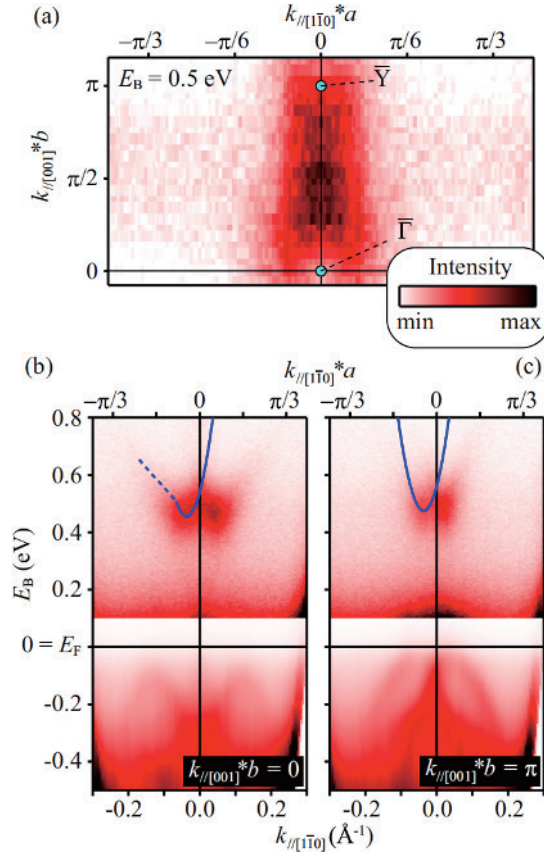


Figure 3. ARPES intensity plots of Bi/GaSb(110)-(2×1) at 25 K taken with two laser pulses. A delay time between the pump and probe pulses was set to 1 ps. The pump pulses ($\hbar\nu = 1.5$ eV) were linearly polarized photons, the electric field vector, which lies in the photon incident plane. The probe ones had the same incident plane as the circular polarization ($\hbar\nu = 6.0$ eV). (a) Constant energy contour at $E_B \sim 0.5$ eV. (b) ARPES intensity plot along $\bar{\Gamma}-\bar{X}$. The photoelectron signals in $E_B > 0.1$ eV are enhanced to make the surface conduction band dispersion visible. (c) Same as (b) but taken along $\bar{Y}-\bar{M}$. Solid and dashed curves in (b) and (c) guide the theoretical band dispersions.

References

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- 2) Y. Ohtsubo, N. Tokumasu, H. Watanabe, T. Nakamura, P. Le Fèvre, F. Bertran, M. Imamura, I. Yamamoto, J. Azuma, K. Takahashi and S. Kimura, *Phys. Rev. B* **101**, 235306 (8 pages) (2020).

Innovative Catalysis Development Based on Radiant Light Spectroscopy

**Division of Advanced Molecular Science
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Education

1993 B.S. Osaka University
1995 M.S. Osaka University
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Professional Employment

1995 JSPS Research Fellow
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2002 Guest Scientist, Scripps Research
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Awards

2001 N.E. CHEMCAT Award in Synthetic Organic Chemistry, Japan
2008 The 22nd Special Young Lecturer in the 88th CSJ Annual Meeting
2012 Theme Chemistry Journal Award
2015 BCSJ Award, The Chemical Society of Japan
2019 BCSJ Award, The Chemical Society of Japan

Member
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HAGIWARA, Hisayo

Keywords Organometallic Catalyst, Peptide-Based Material, X-Ray Spectroscopy

For future sustainable development, we promote research development of advanced catalysts based on element strategy criteria. Non-precious metal such as iron, nickel, cobalt, and copper catalysts are investigated for synthetic transformation of various organic molecules related to pharmaceutical and photoelectronic materials. To elucidate the precise catalytic properties and mechanism, X-ray absorption spectroscopy (XAS) and various radiant light spectroscopies provided at UVSOR are used, where development of a solution-phase in situ XAS spectroscopic techniques and system will be intensively conducted for the study of homogeneous organometallic catalysts. Multidisciplinary research covered on DFT and XAS spectroscopy is also conducted to achieve an efficient structural determination technique being never accessible by the conventional XAS-based structural analysis. Using these cutting-edge spectroscopic technologies, we aim to promote innovative catalyst research which enable us highly efficient

transformation of extremely unreactive organic molecules such as simple aromatic compounds, CO₂, and biomass into valuable functional materials.

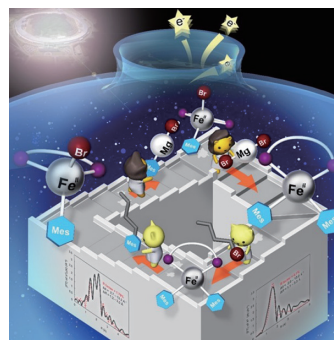


Figure 1. Investigation of iron-catalyzed cross-coupling reactions based on DFT-XAS analysis.

Selected Publications

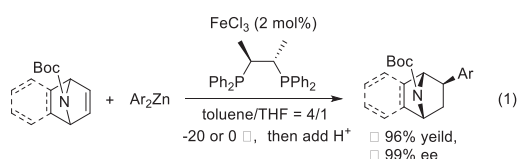
- H. Takaya, S. Nakajima, N. Nakagawa, K. Isozaki, T. Iwamoto, R. Imayoshi, N. Gower, L. Adak, T. Hatakeyama, T. Honma, M. Takagi, Y. Sunada, H. Nagashima, D. Hashizume, O. Takahashi and M. Nakamura, "Investigation of Organoiron Catalysis in Kumada-Tamayo-Corriu-Type Cross-Coupling Reaction Assisted by Solution-Phase X-Ray Absorption Spectroscopy," *Bull. Chem. Soc. Jpn.* **88**, 410–418 (2015).
- R. Agata, H. Takaya, T. Iwamoto, T. Hatakeyama, K. Takeuchi, N. Nakatani and M. Nakamura, "Iron-Catalyzed Cross Coupling of Aryl Chlorides with Alkyl Grignard Reagents: Synthetic Scope and Fe^{II}/Fe^{IV} Mechanism Supported by X-Ray Absorption Spectroscopy and Density Functional Theory Calculations," *Bull. Chem. Soc. Jpn.* **92**, 381–390 (2019).
- Y. Kanazawa, T. Mitsudome*, H. Takaya* and M. Hirano*, "Pd/Cu-Catalyzed Dehydrogenative Coupling of Dimethyl Phthalate: Synchrotron Radiation Sheds Light on the Cu Cycle Mechanism," *ACS Catal.* **10**, 5909–5919 (2020).
- L. Adak, M. Jin, S. Saito, T. Kawabata, T. Itoh, S. Ito, A. K. Sharma, N. J. Gower, P. Cogswell, J. Geldsetzer, H. Takaya, K. Isozaki and M. Nakamura*, "Iron-Catalysed Enantioselective Carbometallation of Azabicycloalkenes," *Chem. Commun.* **57**, 6975–6978 (2021).

1. DFT-XAS-based Mechanistic Investigation of Transition-Metal-Catalyzed Reaction in Homogeneous Phase^{1–4)}

Mechanistic study on transition-metal complex-catalyzed reaction in homogeneous phase mostly carried out by means of solution-phase NMR analysis. However, studies on base metal catalysts being essential for SDGs achievement often suffer from difficulties due to their paramagnetic property which provide unusual large paramagnetic shifts with significant peak broadening. To solve the problems in mechanistic study of base metal-catalyzed reaction, we conducted to use XAS which enables element specific analysis to determine the oxidation state and the geometry of catalytic species without interference from the paramagnetic property.

Recently, we have succeeded to elucidate the mechanism of Pd/Cu-catalyzed oxidative coupling of dimethyl phthalate where the oxidation states and the local coordination geometries of catalytic intermediates were determined under the stoichiometric conditions of each reaction path.^{1,2)} DFT- and single crystal X-ray structural analysis adequately provided the precise molecular structure of these intermediates. This research is the first to provide a clear answer to the long-term debate on the reaction mechanism in the last three decades and demonstrated that XAS is the powerful tool for the mechanistic study on homogeneous paramagnetic transition-metal complex-catalyzed reactions being difficult by means of the conventional solution-phase NMR analysis.

Effectiveness of the DFT-XAS-based mechanistic study on paramagnetic transition-metal complex-catalyzed reaction was clearly demonstrated in iron-catalyzed enantioselective carbometallation of azabicycloalkenes (eq. 1).³⁾ In this study, formation of diphosphine ligand-coordinated tetrahedral iron species, which is a key species for chiral recognition of substrate, was successfully identified with the molecular structure in the reaction mixture.



2. XAFS-Based Structural Study on Flexible Organometallic Systems^{5–7)}

Generally, organometallics bearing highly flexible molecular structure make it difficult to prepare a single crystal bearing sufficient size and quality for X-ray crystallography. We conducted DFT-XAS-based structural analysis of such flexible molecule. Recently, Prof. Uemura and Benjamin found a flexible MOF prepared from $[\text{Zn}_2(\text{BDC})_2(\text{DABCO})]_n$ and polystyrene which has a polymer-threaded multi-layered structure after removing the DABCO pillar ligand. The polymer-threaded extremely flexible molecular scaffolds showed no

clear diffraction pattern except for a broad peak. To determine the molecular structure of this flexible MOF system, we carried out Zn K-edge and O K-edge XAS. A DFT-based simulation of both XAS spectra clearly demonstrated that $[\text{Zn}_2(\text{BDC})_2]_n$ -monolayer was preserved well in the turbostratic phase without DABCO pillar.⁴⁾

Another successful application was achieved in the structure determination of double-decker type iron porphyrin/phtalocyanine dimer in which two units of iron-porphyrin or phtalocyanine were interlocked through highly flexible quadruplet axials or iron-oxo linkage.^{5,6)} Fe K-edge XAS-based structural analysis supported with DFT-MD-based simulation successfully provides the precise local coordination geometry of iron centers in highly flexible supramolecular system.

Another successful example of the DFT-XAS-based structural study was demonstrated by the molecular structure determination of an anionic homoleptic organo-transition metal complex of $[\text{Li}(12\text{-crown-4})_2][\text{MPh}_6\{\text{Li}(\text{thf})_2\}_2]$ ($\text{M} = \text{Rh}$ and Ir) in THF solution which are the first examples of hexaaryl complexes of d6 metals with a partially contacted ion pair structure of $\text{Ir}^{2-}\text{-Li}^+$ in solution-phase.⁷⁾

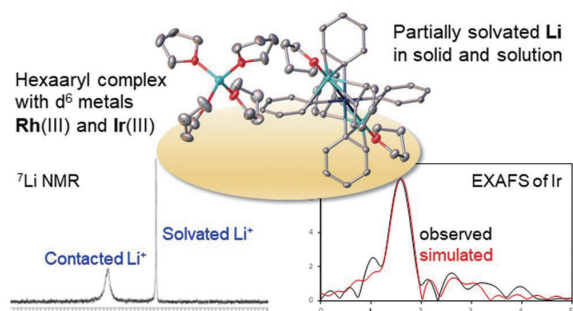


Figure 2. The molecular structure determination of $[\text{Li}(12\text{-crown-4})_2][\text{MPh}_6\{\text{Li}(\text{thf})_2\}_2]$.

References

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- 3) L. Adak, M. Jin, S. Saito, T. Kawabata, T. Itoh, S. Ito, A. K. Sharma, N. J. Gower, P. Cogswell, J. Geldsetzer, H. Takaya, K. Isozaki and M. Nakamura*, *Chem. Commun.* **57**, 6975–6978 (2021).
- 4) L. O. Benjamin, H. Takaya and T. Uemura*, *J. Am. Chem. Soc.* **141**, 14549–14553 (2019).
- 5) Y. Yamada*, K. Morita, T. Sugiura, Y. Toyoda, N. Mihara, M. Nagasaka, H. Takaya, K. Tanaka, T. Koitaya, N. Nakatani, H. Ariga-Miwa, S. Takakusagi, Y. Hitomi, T. Kudo, Y. Tsuji, K. Yoshizawa and K. Tanaka*, *ChemRxiv* DOI: 10.26434/chemrxiv.14728860.v1 (2021).
- 6) N. Mihara, Y. Yamada*, H. Takaya, Y. Kitagawa, K. Igawa, K. Tomooka, H. Fujii and K. Tanaka*, *Chem. –Eur. J.* **25**, 3369–3375 (2019).
- 7) T. Iwasaki*, Y. Hirooka, H. Takaya, T. Honma and K. Nozaki*, *Organometallics* **40**, 2489–2495 (2021).