ACT-C

Creation of Advanced Catalytic Transformation for the Sustainable Manufacturing at Low Energy, Low Environmental Load

Advanced Catalytic Transformation program for Carbon utilization

2016-2017

Japan Science and Technology Agency

ACT-C

Creation of Advanced Catalytic Transformation for the Sustainable Manufacturing at Low Energy, Low Environmental Load

Outline of the Research Area

This research area aims to create an advanced catalytic transformation that can contribute to solving various challenges by realizing a low-carbon society, and producing sustainable and advanced drugs and functional materials. Specifically, the following studies are addressed:

1) Studies of reactions (such as CO_2 reduction) to utilize small molecules as a resource instead of fossil resources and efficiently convert the CO_2 into useful C1, C2 and C3 compounds;
2) Studies of reactions such as asymmetric carbon-carbon bond formation, which will lead to industrial applications;
3) Studies of the creation of π(pi)-electron molecules having superior properties and functions by innovative bond formation, cleavage and recombination; and the creation of new features by introducing functional groups to the pi-electron molecules.

As such molecular conversion methods aim to be safe, with high atom efficiency, high yield and high selectivity, ACT-C promotes challenging research beyond the boundaries of the field of chemistry, physics, mathematics and engineering. In addition, cooperation with research related to measurement and analysis as well as theoretical chemistry, for the elucidation of reaction mechanism is encouraged.

Objectives of the Research Area

- Creation of a reduction method for transforming and applying CO_2 as a useful substance
- Creation of a catalytic substance transformation technology that directly generates asymmetric carbon-carbon bonds, and does so with high yield, effectiveness, selectivity, economy, and safety
- Chemosynthesis of π-electron molecules and creation of new function generation approaches for devices

Features of Research Area Management

1. Research Progress Monitoring

The Research Supervisor and Advisors review research progress every quarter and provide various types of advice for each project. In addition, the research framework and resources are re-examined and flexibly revised depending on research progress.

2. Networking and Exchange of Research Progress

Research progress is presented and discussed at ACT-C meetings every year, where all PIs, the Research Supervisor, Principal Program Director, and Advisors participate, to share ideas and to build inter-disciplinary research networks.

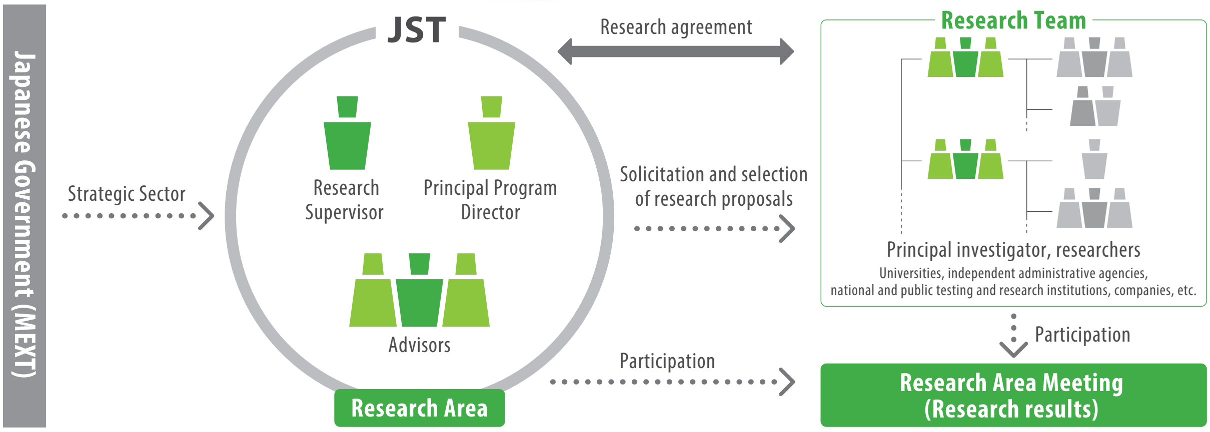
3. Promoting Synergistic Collaboration

Through ad hoc workshops and symposium on specific themes, intra- and inter- research collaborations are promoted to enhance synergistic effects.

Summary

The Strategic Sector	Creation of advanced catalytic transformation techniques/technologies for addressing the priority issues such as environment, energy, drug discovery and others
Research Period	5 years
Budget	40~300 million JPYen/Project
Research Projects	51 projects

Research Framework



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A Study on Bio-Mimetic Catalysis Using Mesoporous Organosilica

01

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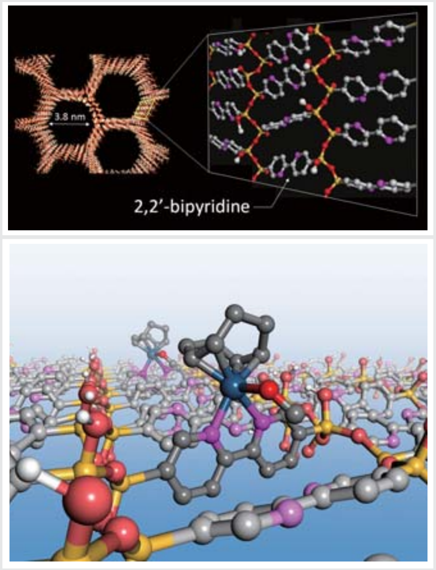
Development of new catalysts for efficient conversion of abundant small molecules such as CO_2, H_2O, and N_2 into fuel and resources is one of the most important challenges we should overcome in the near future in order to free ourselves of the oil dependency. In this project, we will attempt to mimic the essences of bio-functions of enzymes and photosynthesis, which converts such small molecules at ambient conditions, using highly ordered organic-based nanoporous materials as a scaffold.



1 Synthesis of periodic mesoporous organosilica with bipyridine ligand in the framework

Synthesis of a solid chelating ligand for the formation of efficient heterogeneous catalysts is highly desired in the fields of organic transformation and solar energy conversion. Here, we report the surfactant-directed self-assembly of a novel periodic mesoporous organosilica (PMO) containing 2,2′-bipyridine (bpy) ligands within the framework (BPy-PMO) from a newly synthesized organosilane precursor $[(i\text{-PrO})_3\text{Si-C}_{10}\text{H}_6\text{N}_2\text{-Si(O}i\text{-Pr)}_3]$ without addition of any other silane precursors. BPy-PMO had a unique pore-wall structure in which bipyridine groups were densely and regularly packed and exposed on the surface. The high coordination ability to metals was also preserved. BPy-PMO showed excellent ligand properties for heterogeneous metal catalysis resulting in superior activity, durability, and recyclability to the homogeneous analogous metal catalyst. BPy-PMO has the great potential as a solid chelating ligand and a useful integration platform for construction of efficient molecular-based heterogeneous catalysis systems.

2 Heterogeneous catalysis for direct C-H borylation of arenes using BPy-PMO

We found that Ir complex immobilized on BPy-PMO showed efficient heterogeneous catalysis for direct C–H borylation of arenes and heteroarenes in the combination of pinacolborane (HBpin) or bis(pinacolato)-diboron (B_2pin_2). The precatalyst could be handled without the use of a glove box. The catalyst was easily recovered from reaction mixtures by simple filtration under air. The recovered catalyst still showed good catalytic activity for at least three more times for the borylation of benzene. The system using Ir-BPy-PMO and HBpin was also utilized in syntheses of multi-boronated thiophene-based building blocks containing ladder-, acenefused-, and fused-thiophene skeletons. The combination of a stable and reusable solid catalyst and inexpensive HBpin is expected to be superior to conventional approaches for the development of industrial applications.

3 Synthesis of periodic mesoporous organosilica with molecular-scale ordering self-assembled by hydrogen bonds

Nanoporous materials with functional frameworks have attracted attention because of their potential for various applications. Silica-based mesoporous materials generally consist of amorphous frameworks, whereas a molecular-scale lamellar ordering within the pore wall has been found for periodic mesoporous organosilicas (PMOs) prepared from bridged organosilane precursors. Formation of a “crystal-like” framework has been expected to significantly change the physical and chemical properties of PMOs. However, until now, there has been no report on other crystal-like arrangements. We found a new molecular-scale ordering induced for a PMO. Our strategy is to form pore walls from precursors exhibiting directional H-bonding interaction. We demonstrate that the H-bonded organosilica columns are hexagonally packed within the pore walls. We also show that the H-bonded pore walls can stably accommodate H-bonding guest molecules, which represents a new method of modifying the PMO framework.

Materials Design of Composite Structure in Nano-Scale and its Application to CO_2 Utilization

02

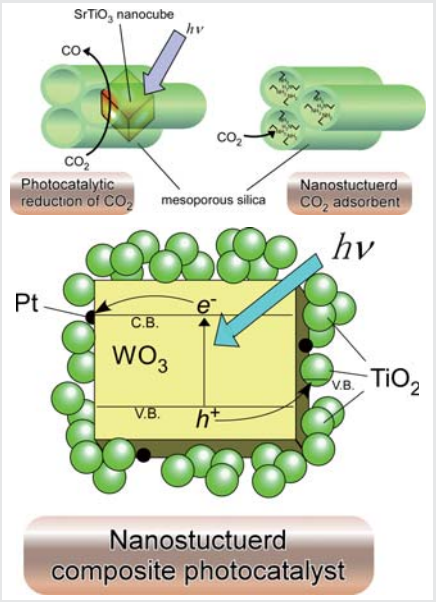
Principal Investigator (PI)

Kei INUMARU
Professor, Graduate School of Engineering, Hiroshima Univeristy

In this study, composite structures of materials are designed in nano-scale by using nanocrystals and nanospaces of porous materials. The composite materials are applied to CO_2 separation, and utilization by catalysis and photocatalysis. The scope of this study includes design of nanocrystals catalysts and nanocrystals – porous material composites for photoreduction of CO_2, utilization of CO_2 as a source material of useful carbonates, and separation of CO_2 by adsorbents with tuned nanostructures.

1 Metal oxide nanoparticles – mesoporous silica nanocomposite photocatalysts for CO_2 reduction

Nanocrystals exposing particular crystal planes are promising materials for catalysis and photocatlysis. Strontium titanate ($SrTiO_3$) nanocube-dispersed mesoporous silica was prepared for the first time. Oleate-modified $SrTiO_3$ nanocubes with diameter of ca. 10 nm were synthesized by a hydrothermal process. The nanocubes were embedded into mesoporous silica, aided by the high affinity of surface oleyl groups with surfactants employed as templates of the mesoporous silica. Nanocubes within the nanocomposite maintained their shape and size without fusion or sintering, even after calcination at 1073 K. The nanocomposite exhibited high photocatalytic activity in the decomposition of methylene blue because of the combination of preferential molecular adsorption by mesoporous silica and photocatalysis by $SrTiO_3$. Then, this material was applied to photocatalytic reduction of CO_2. It was revealed that CO was produced under UV irradiation.



2 Enhanced photocatalytic activity of nanostructured photocatalyst with designed contacts between metal oxide particles

A composite structure in which larger metal oxide crystalline particles of WO_3 (ca. 200 nm) were surrounded by metal oxide nanoparticles of TiO_2 (ca. 6 nm) was designed to achieve highly active photocatalysis. This composite structure allows hole transfer from the valence band of WO_3 to that of TiO_2, which likely suppressed electron–hole recombination and enabled the oxidation reaction to take place on the surface of the TiO_2 particles. An electrostatic adsorption approach was used to construct this composite structure. Positively and negatively charged polymers were alternately adsorbed onto crystalline large crystalline particles of WO_3 via a layer-by-layer assembly, followed by adsorption of TiO_2 particles on the surfaces of WO_3. After calcination to remove the adsorbed polymer layers, Pt particles were dispersed on the composite structure by photodeposition. The resulting Pt/WO_3–TiO_2 composite photocatalyst showed a higher rate of activity towards the photocatalytic decomposition of gaseous organic molecules under visible light irradiation compared with that of Pt/WO_3. Pt/WO_3–TiO_2 also converted the organic molecules to CO_2 almost completely, whereas the amount of CO_2 produced over Pt/WO_3 was much smaller than that expected for the complete oxidation of the organic molecules. These results highlight a promising strategy for designing interfaces between different oxide particles to achieve nanostructures with high performances.

3 Controlling CO_2 adsorption properties of amino group grafted mesoporous silica by changing the pore size of mesoporous silica: control of spatial vicinity of functional groups in the nanospaces.

Materials were synthesized by grafting organic amino groups on the pore walls of mesoporous silica with different pore size. CO_2 adsorption properties of these materials were examined. Reversible and irreversible adsorption was measured in a wide range of CO_2 concentration. For this kind of adsorbates, one CO_2 molecule and two amino groups react to form ammonium – carbamate ion pair species, so the neighboring two amino groups act as a adsorption site. It was found that materials prepared by using mesoporous silica with smaller pore size showed high CO_2 adsorption amount per organic chain. These results were explained by a novel principle that the degree of 3-dimensional spatial vicinity of amino functional groups could be controlled by changing pore diameter of mesoporous silica.

Synthesis of Acrylic Acid from Ethylene or Acetylene Based on the Innovative Transition Metal Catalysis

03

Principal Investigator (PI)

Nobuharu IWASAWA
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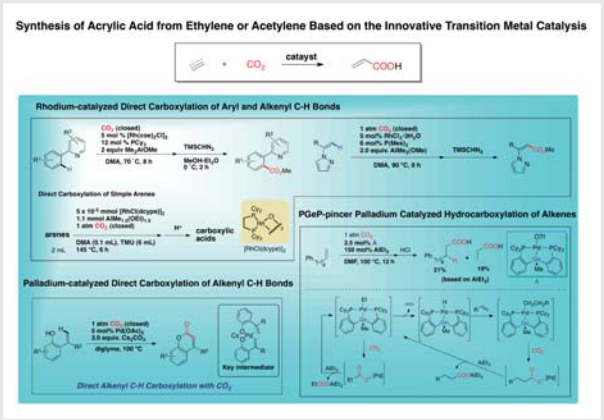
Catalytic carbon dioxide fixation reactions with carbon-carbon bond formation will be realized based on the development of innovative transition metal complexes. Various new carboxylation reactions along with utilization of easily available reducing agents such as formate, alcohols, and hydrogen, and even photoexicted electron will be achieved to realize preparation of saturated and α, β-unsaturated carboxylic acids. As a final goal of this project, preparation of acrylic acid from ethylene or acetylene will be realized.



1 Rhodium(I)-Catalyzed Direct Carboxylation of sp$_2$ C-H Bonds

Direct C-H carboxylation of aryl and alkenyl substrates containing a directing group was realized under atmospheric pressure of CO_2 using a catalytic amount of a rhodium complex in combination with a stoichiometric methylaluminum reagent. The reaction proceeded with various arylpyridines and alkenylpyrazoles to give the corresponding carboxylic acids in good yield. Based on these results, the direct carboxylation of simple arenes under atmospheric pressure of CO_2 was examined. Extensive screening of the ligand and reaction conditions revealed that isolated 1,2-bis(dicyclohexylphosphino)ethane-rhodium(I) chloride complexes showed catalytic activity for the carboxylation of benzene in the presence of $AlMe_{1.5}(OEt)_{1.5}$ and the TON of 40 was achieved by addition of DMA and TMU. The reaction showed wide generality and various arenes such as toluene, xylene, electron rich or electron deficient benzene derivatives, and heteroaromatics are directly carboxylated with high TON. This rhodium-catalyzed protocol demonstrates a new approach toward direct carboxylation of simple arenes utilizing CO_2 as a C1 source.

2 PGeP-pincer Palladium Complex-Catalyzed Hydrocarboxylation of Unsaturated Hydrocarbons

Based on the PSiP-pincer palladium complex developed in our laboratory for the catalytic hydrocarboxylation of allenes and 1,3-dienes, the hydrocarboxylation reaction of alkenes and alkynes was examined. It was found that a PGeP-pincer palladium complex showed promising activity and stability in this reaction, and reasonable catalytic activity was realized by carrying out the reaction in the presence of a catalytic amount of the PGeP-pincer palladium complex with Et_3Al as a stoichiometric reductant under atmospheric pressure of CO_2. Although the TON was not very high, the reaction showed reasonable generality. In addition, use of formate salts as a hydride as well as a CO_2 source was achieved in a PGeP-palladium complex-catalyzed hydrocarboxylation of allenes through a highly efficient decarboxylation-carboxylation process. This reaction proceeded under mild conditions and provides an alternative strategy for utilizing formate salts as a C1 source. The reaction displayed broad functional group compatibility, with alcohol, amide, aldehyde and ketone substituents tolerated.

3 Palladium(II)-Catalyzed Direct Carboxylation of Alkenyl C-H Bonds

Palladium-catalyzed direct carboxylation of alkenyl C-H bonds of 2-hydroxystyrenes with CO_2 was realized. Treatment of 2-hydroxystyrenes and a catalytic amount of $Pd(OAc)_2$ with Cs_2CO_3 under atmospheric pressure of CO_2 afforded coumarins as the carboxylation products in good yield. The use of Cs_2CO_3 as base is crucial for the success of this reaction. The reaction showed reasonable generality to give various synthetically useful coumarin derivatives in good yield. Furthermore, isolation of the key alkenylpalladium intermediates obtained via C-H bond cleavage was achieved. In this reaction, alkenyl-palladium complex is generated by chelation-assisted alkenyl C–H bond cleavage of 2-hydroxystyrene with $Pd(OAc)_2$ along with coordination of the second molecule of 2-hydroxystyrene as its cesium salt. Subsequently, this complex is proposed to undergo reversible carboxylation reaction with CO_2, and the third molecule of 2-hydroxystyrene can react with the palladium carboxylate intermediate in the equilibrium of the reversible carboxylation reaction to give coumarin with regeneration of the complex. This is the first example of Pd(II)-catalyzed alkenyl C–H bond functionalization with nucleophilic carboxylation.

Alcohol Synthesis Based on CO_2 Reduction at Polymer Electrolyte Fuel Cell Cathode

04

Principal Investigator (PI)

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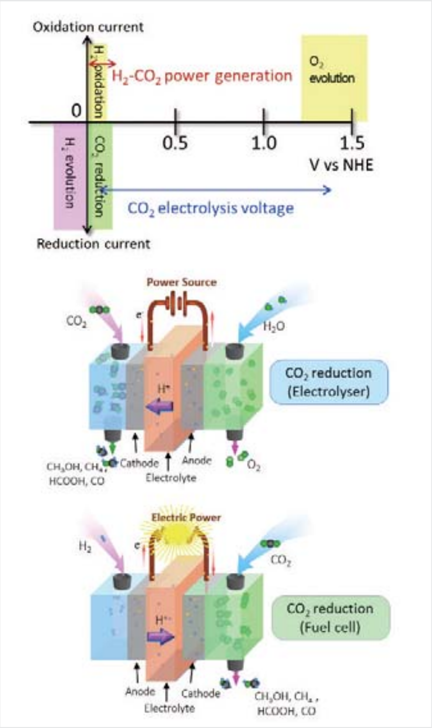
This project aims to develop a new technology that efficiently converts carbon dioxide to alcohol or further reduced materials around theoretical electrode potential of polymer electrolyte fuel cell (PEFC) cathode without using high pressure or high temperature. Investigation of the CO_2 reduction around the theoretical potential will lead to an H_2-CO_2 PEFC that generates an electric power by reducing the CO_2. Key technologies for realizing the purpose are (i) improvement of membrane electrode assembly (MEA), (ii) development of new electrocatalysts, and (iii) cell operation of the H_2-CO_2 PEFC power generation.



1 CO_2 reduction at a Pt-based MEA cathode

CO_2 electroreduction performances are investigated at Pt/C- and Pt-Ru/C-based MEAs in a single cell. Cyclic voltammograms were measured under N_2 and CO_2 atmospheres using the Pt/C- and Pt-Ru/C-based MEA. A typical voltammogram attributed to the Pt electrode has been obtained using Pt/C under an N_2 atmosphere, and an extra oxidation peak appeared at 0.60 V vs. DHE (dynamic hydrogen electrode) under a CO_2 atmosphere. This peak has been considered to be caused by the re-oxidation of the CO_2 reductant. For the Pt-Ru/C, the re-oxidation peak has been observed at 0.50 V vs. DHE which is more negative than Pt/C. The limiting cathode potential of the cyclic voltammogram was changed from 0.06 to 0.35 V vs. DHE under a CO_2 atmosphere, and the magnitude of the re-oxidation peak decreased. The CO_2 reduction occurred at coulombic efficiency of 75%, whereas a generation efficiency of methane as a product detected in the exhausted gas was 1% at the Pt-Ru/C. These ensure that the CO_2 reduction takes place at 0.06 to 0.3 V vs. DHE and that the reduction product strongly adsorbs on the electrode.

2 Power generation at H_2-CO_2 fuel cell

The possible power generation of a PEFC has been investigated by feeding H_2 and CO_2 to the anode and cathode, respectively. First, a PEFC consisting of a Pt/C-based anode and cathode was fabricated, and the polarization curves during flowing H_2, O_2, and CO_2 were measured with respect to the DHE. Next, the onset potentials of the polarization curves were compared. The onset potential of the CO_2 reduction reaction is higher than that of the H_2 oxidation reaction (HOR), which well agrees with the PEFC power generation principle. Also, the onset potential of the CO_2 reduction is theoretically supported by the standard electrode potentials of reactions in which CO_2 participates. As a result, the H_2-CO_2 PEFC successfully generated electric power, which indicates that CO_2 participate in the power generation by being reduced. The generated power increases with an increase in the cell temperature of the H_2-CO_2 PEFC, suggesting that the CO_2 electroreduction is thermally activated. Under the controlled potential of 0.051 V vs. DHE, the cathode current of the H_2-CO_2 PEFC changed with a 2 h cycle, implying that the cathode Pt is poisoned by the CO_2 reduction product and then recovered.

3 CO_2 redox properties at a PEFC electrode

Reformed H_2 gas containing a small amount of CO and 10-30% CO_2 degrades the performance of PEFCs. CO_2 is known to be reduced at the Pt electrode at 0.06-0.30 V vs. DHE which corresponds to the anode potential of the PEFC. However, the relationship between the performance degradation of the PEFC and the reactivity of CO_2 has not been clarified. The reactivity of CO_2 and the adsorption of its reductant were investigated by employing Pt-Ru/C-based MEAs which include the Pt-Ru/C (Pt:Ru=1:0, 1:1, and 2:3 in atomic ratio) electrocatalyst under a pure CO_2 atmosphere. As a result, it was found that the CO_2 could be easily reduced at the Pt-Ru/C electrocatalyst at 0.06-0.30 V vs. DHE which was equivalent to the anode potential of the PEFC. Moreover, the reactivity of the adsorbed CO_2 reductant was changed by the addition of Ru and increasing the cell temperature. Consequently, the most suitable anode catalyst among three kinds of catalysts examined was $Pt_{0.4}Ru_{0.6}/C$, which could easily desorb the CO_2 reductant.

Development of Interfacial-Morphology Controlled Photocatalytic Electrode toward CO_2 Conversion

05

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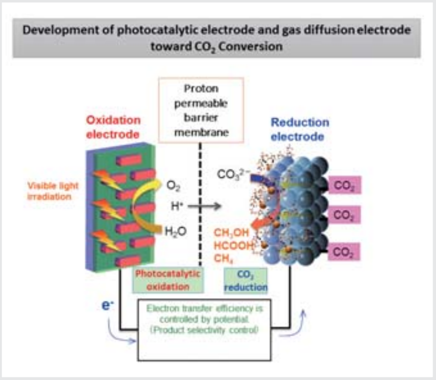
In the present project, our quadripartite team addresses the challenge of efficient conversion of CO_2 by using newly-developed morphology controlled TiO_2 photocatalysts nanoparticles, hybrid photocatalysts composed of g-C_3N_4 and WO_3 and p-type photocatalytic electrode under wide range of irradiation. The conversion efficiency of CO_2 reduction over the photocatalysts might increase by exposing a finely controlled crystal surface, controlling band structure of nanocomposite photocatalysts and development of new p-type semiconductor nanomaterials with a high conduction band potential. In addition, the development of photoelectrochemical system equipped with gas diffusion electrodes results in a high efficient photoelectrode systems, which perform CO_2 conversion into valuable compound such as alcohol under wide range of irradiation.



1 Development of Morphology controlled TiO_2

Morphology controlled TiO_2 having anatase or brookite phase was successfully prepared. Reactivity of each exposed crystal surface was evaluated showing different reactivity such as reduction and oxidation, respectively. These properties achieve a high charge separation and improvement of a high photocatalytic activity. These photocatalysts showed a rather high photocatalytic activity for CO_2 reduction to generate methanol as a main product under UV light irradiation. The apparent quantum efficiency for the reaction was reached to around 1.0 %. Several kinds of metal compounds such as Au, Ag, and Rh were loaded as a co-catalyst only on the reduction sites of exposed crystal surface controlled TiO_2 nanorod having brookite phase by photodeposition technique. The photocatalytic activity of the co-catalysts loaded brookite TiO_2 nanorod drastically increased. Among the co-catalysts loaded TiO_2 photocatalysts, brookite TiO_2 nanorod loaded with Rh show the highest activity. The quantum efficiency of Rh loaded brookite TiO_2 nanorod is about 2.8%.

2 Development of nanocomposite photocatalyst a composed of g-C_3N_4 and WO_3

A nanocomposite photocatalyst composed of visible light responsive g-C_3N_4 and WO_3 was prepared by planetary mill treatment. Photocatalytic reduction of CO_2 proceeded over the nanocomposite photocatalyst under visible light irradiation. The quantum efficiency of the reaction is around 0.15 %. The main product of the reaction over nanocomposite photocatalytic systems is also methanol. Several kinds of metal compounds such as Au and Ag were loaded as a co-catalyst only on the surface of g-C_3N_4 for improvement photocatalytic activity. After preparation of metal co-catalyst loaded g-C_3N_4, nanocomposite photocatalyst was prepared by using same technology. The photocatalytic activity of the co-catalysts loaded nanocomposite increased. Among the co-catalysts nanocomposite photocatalysts, Ag loaded nanocomposite photoctalysts show the highest activity. The quantum efficiency of Rh loaded brookite TiO_2 nanorod is about 0.2 %.

3 Development of boron doped g-C_3N_4 photoelectrodes

Graphitic carbon nitride (g-C_3N_4) and boron-doped g-C_3N_4 (B-doped g-C_3N_4, BCNx) were prepared by heating melamine and a mixture of dicyanodiamide and BH_3NH_3, respectively. The photocurrent response of B-doped g-C_3N_4 was about 5-times larger than that of pure g-C_3N_4. B-doped g-C_3N_4 coated with Rh as a co-catalyst showed the highest photocurrent response under solar light irradiation, its photocurrent being about 10-times larger than that of original g-C_3N_4. Under photoelectrochemical conditions, we also observed the products in gas phase and aqueous phase. C_2H_5OH was observed as a main product, while small amounts of CO and H_2 were observed in gas phase. The solar light conversion efficiency of the main product is about 0.02 %.

5 Development of new p-type semiconductor photoelectrodes

We also developed new p-type photoelectrodes materials for CO_2 reduction under solar light. Several kinds of p-type photoelectrodes materials such as $CuCrO_2$ and $Cu_3Nb_2O_8$ have already found. Although, the photocurrent response of $Cu_3Nb_2O_8$ is 30-40 times larger than that of g-C_3N_4, the stability of $Cu_3Nb_2O_8$ is not good because Cu^{2+} ions were easily reduced under solar light irradiation. We will continue to investigate the key technology for stabilization of these electrodes and new p-type photoelectrodes materials for high efficient CO_2 reduction under solar light.

Asymmetric Cycloaddition via Nickelacycles

06

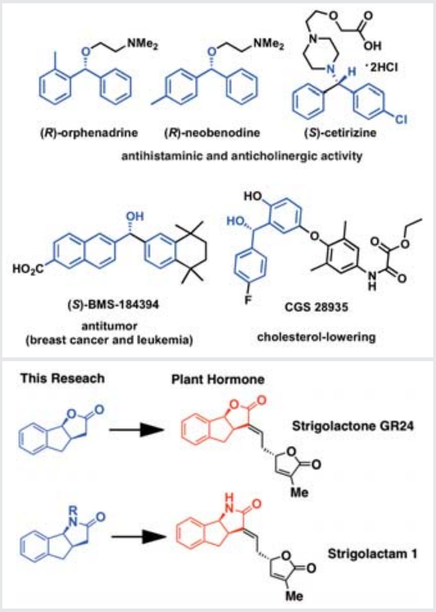
Principal Investigator (PI)

Sensuke OGOSHI
Professor, Osaka University

The formation of "carbon-carbon bond" is a momentous issue in the organic synthesis because carbon is a ubiquitous atom. Carbon atom has four hands and the selective shaking hand between two carbon atoms with high enantio selectivity is very challenging due to the versatility of the optically active organic compounds. In fact, the enantioselective carbon-carbon bond forming reactions are much less reported than the enantioselective carbon-hydrogen bond forming reactions. In this project, we try to design and synthesize new smart organo-transition metal complexes that allow us to develop new enantioselective carbon-carbon bond forming reactions.

1 Asymmetric Synthesis of Benzoxasilole

Diphenyl methanols are useful synthetic intermediates for the synthesis of a variety of bioactive organic compounds. Thus, so far, a lot of synthetic methods of the diphenyl methanols have been reported. In this research, we found that an asymmetric nickel(0) complex catalyst with asymmetric NHC Ligand can promote the migration of an aryl group from silicon to the aldehyde carbon to give a variety of optically active benzoxasiloles in high yield and high enantiomer excess. This reaction can be applied to the synthesis of a variety of benzoxasiloles. Moreover, these optically active benzoxasiloles can be converted to the corresponding optically active diphenyl methanols in one step. The bioactive organic compounds that can be prepared from the optically active diphenyl methanols are listed below. In addition, the benzoxasiloles can be applied to the Hiyama coupling reaction in the presence of palladium catalyst to give the corresponding optically active diaryl compounds.



2 Intramolecular Carbonylative Cycloadditions

An intramolecular carbonylative cycloaddition is an efficient method to synthesize cyclic carbonyl compounds and a lot of transition metal catalysts have been reported. However, only a limited number of transition metals allow us to synthesize lactones and lactams, since the formation of oxa- or aza-metalacycles is required for the carbonylative cycloaddition. Nickel is a promising transition metal to achieve the synthesis of lactones and lactams in one step by carbonylation. We have developed nickel-catalyzed carbonylation reactions to give tricyclic lactones and lactams that enable short steps the synthesis of strigolactones and storigolactams. The strigolactones have been reported as a plant hormone in 2009. Then sterigolactams have been reported that they play more effective than strigolactones as a plant hormone in 2014. However, we haven't known well the effect of the strigolactones and sterigolactams as a plant hormone. Thus, a short steps synthesis of strigolactones and sterigolactams is required to promote the research of the effect on the plants. This research project achieves a short steps synthesis of strigolactones and sterigolactams.

3 Asymmetric [2+2+2] Cycloaddition of Two Enones with An Alkyne

The diastereo-selective construction of a cyclohexene with four stereogenic centers is one of the attractive and challenging targets in organic synthesis because there are eight isomers that can be generated. Furthermore, the corresponding selective asymmetric reactions are more difficult and challenging because the selective synthesis of one enantiomer out of twice the number of possible isomers. In this project, we have developed nickel-catalyzed asymmetric [2+2+2] cycloaddition of two enones with an alkyne to give optically active hexa-substituted cyclohexenes in one step. The key to success of the reaction is the selection of appropriate chiral NHC ligand. The absolute stereochemistry was determined by the correlation of CD spectra and calculation based on the ratio of the all-possible conformers, which is recognized recently as a reliable method for the determination of stereochemistry. In addition, calculations on its reaction mechanisms will show us how to optimize the reaction conditions.

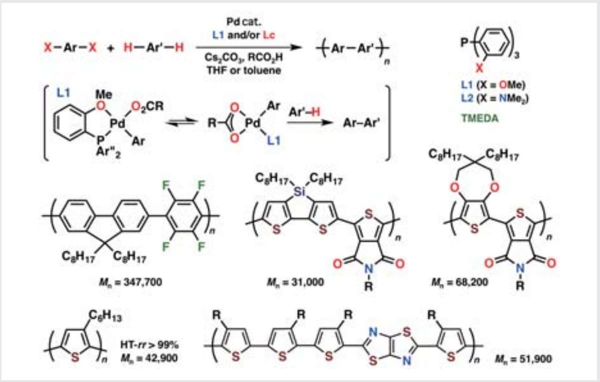
Development of Highly Efficient Catalysts for Synthesizing π-Conjugated Polymers via Direct Arylation

07

Principal Investigator (PI)

Fumiyuki OZAWA
Professor, Kyoto University

π-Conjugated polymers consisting of heteroaromatic rings have found wide application in optoelectronic devices such as photovoltaic cells and field-effect transistors. It has been recognized that π-conjugated polymers are advantageous over small organic molecules in terms of accessibility of thin films and thus enable low-cost fabrication of large-area devices via solution processes. The objective of this research subject is the development of a novel catalytic polymerization process via C–H bond activation (direct arylation polymerization: DArP), which realizes an easy yet efficient method of synthesizing π-conjugated polymers.



1 Development of a Highly Efficient Catalyst for the Synthesis of Donor-Acceptor Polymers

We have developed a highly active catalyst that produces donor-acceptor polymers containing thieno[3,4-*c*]pyrrole-4,6-dione (TPD) or thiazolo[5,4-*d*]thiazole (TzTZ) units (M_n = 18,900–88,100) via palladium-catalyzed direct arylation polymerization (DArP) in quantitative yields. The reactions proceed smoothly in THF and toluene, and the catalyst loading is reduced to 1/5–1/10 compared with conventional cross-coupling polymerizations. The catalyst may be simply in situ generated from $Pd_2(dba)_3$, $P(2\text{-}MeOC_6H_4)_3$ (**L1**), and pivalic acid; all components are commercially available. Detailed mechanistic examinations using $[PdPh(\mu\text{-}O_2CMe)(\mathbf{L1})]_2$ (**1**) as a model compound of catalytic intermediate have revealed that, while complex **1** adopts a dimeric structure in the solid state, it is completely dissociated into $[PdPh(O_2CMe\text{-}\kappa^2 O)(\mathbf{L1})]$ (**2**) as a monomeric species in solution. Monomeric complex **2** possesses extremely high reactivity towards C–H bond activation. The newly developed catalyst realizes versatile synthetic means of π-conjugated polymers without the use of organometallic monomers, which are often laborious in preparation.

2 Development of a Highly Selective Catalyst for the Synthesis of Poly(3-hexylthiophene)

We have developed a novel palladium catalyst that converts 2-bromo-3-hexylthiophene into head-to-tail regioregular poly(3-hexylthiophene) (HT-P3HT; M_n = 30,000–40,000) in almost perfect regioregularity (>99%); the value is superior to that previously achieved by nickel-catalyzed cross-coupling polymerization (up to 98%), and the resulting polymer exhibits higher charge carrier mobility. The catalyst is in situ prepared from the Herrmann-Beller complex and $P(2\text{-}Me_2NC_6H_4)_3$ (**L2**) or TMEDA. All catalyst components are commercially available, and the catalytic performance is easily reproduced. The molecular weight in the catalytic system using **L2** increases linearly with monomer conversion from the middle stage of polymerization, giving HT-P3HT with relatively narrow molecular-weight distribution (M_w/M_n = 1.5–1.6). Detailed analysis of the reaction courses has indicated the occurrence of a living-like chain-growth process, which is initiated from oligomers (P_n = 3.3) generated in the early stage of polymerization. These findings open up new possibilities of direct arylation polymerization, including the synthesis of block copolymers.

3 Development of Mixed-Ligand Catalysts for Preventing Structural Defect Formation

A novel mixed ligand catalyst for palladium-catalyzed direct arylation polymerization (DArP) of 2,6-diiododithienosilole (DTS-I_2) and thienopyrroledione (TPD-H_2) to give poly(DTS-*alt*-TPD) has been developed. It has been documented that this monomer combination has a marked tendency to form homocoupling and branching defects in polymer chains, and the latter defects eventually lead to the formation of insoluble materials. We have demonstrated that the combined use of $P(o\text{-}MeOC_6H_4)_3$ (**L1**) and TMEDA as ligands effectively prevents the defect formation. The side reactions that afford structural defects constitute a sequential process triggered by the reduction of DTS-I units. TMEDA as a simple diamine effectively inhibits the reduction of DTS-I units, giving poly(DTS-*alt*-TPD) (M_n^{GPC} = 20,000) in high cross-coupling selectivity (99%).

Developments of Innovative Synthetic Methods of n-type Organic Semiconductor Materials Using Unreactive Carbon Bonds and Organic Field-Effect Transistor Fabrication Methods

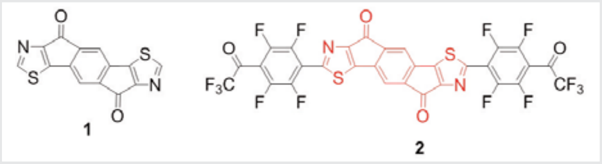
08

Principal Investigator (PI)

Fumitoshi KAKIUCHI
Professor, Keio University of Chemistry

Co-PI

Yutaka IE
Associate Professor, Osaka University



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2

Polycyclic aromatic hydrocarbons (PAHs) are known to have high potential as organic electronic materials. In this project, we will develop new synthetic methods of π-conjugated polycyclic aromatic hydrocarbons which are applicable to n-type semiconductors by means of C-H and other unreactive carbon bonds cleavage. We will fabricate n-type field effect transistor devices using these synthesized compounds. In addition, we will prepare new π-conjugate systems bearing efficient electron-withdrawing functional groups as an electron-accepting terminal unit.

1 Development of New Strategies for Convenient Syntheses of tetrabenzo[*a,d,j,m*]coronenes, dibenzo[*h,rst*]pentaphenes, and dibenzo[*fg,qr*]pentacenes

We have been investigating development of new strategies for short syntheses of polycyclic aromatic hydrocarbons (PAHs) having n-type semiconductor properties by ruthenium-catalyzed ortho arylation of aromatic ketones. A ruthenium-catalyzed coupling reaction of anthraquinones with arylboronate gave 1,4,5,8-tetaraarylanthraquinones. Tetrabenzo[*a,d,j,m*]coronenes, which are one of our target molecules, were obtained by conversion of the carbonyl groups of the 1,4,5,8-tetraarylanthraquinones to methylidenes followed by dehydrogenative aromatization using $FeCl_3$. Dibenzo[*h,rst*]pentaphenes and dibenzo[*fg,qr*]pentacenes were synthesized by chemoselective ruthenium-catalyzed C-O arylations of 1,4- and 1,5-dimethoxyanthraquinones with arylboronates. A reaction of 1,4-dimethoxyanthraquinone with arylboronate using a ruthenium catalyst gave 1,4-diarylanthraquinone via C-O arylation. The diaryltion product was converted to diepoxide compounds by Corey-Chaykofsky reaction. Dehydrative aromatization of the obtained diepoxide compounds using a Lewis acid catalyst provided dibenzo[*h,rst*] pentaphene. Dibenzo[*fg,qr*]pentacenes were also synthesized from 1,5-dimethoxyanthraquinone by using the same procedure employed for the synthesis of dibenzo[*h,rst*]pentaphenes. Instead of arylboronate, when heteroarylboronates were used for the C-O arylation, heteroaromatic rings containing dibenzo[*h,rst*]pentaphene and dibenzo[*fg,qr*]pentacen were obtained.

2 Development of Ruthenium-catalyzed Cross-coupling Reactions of Aromatic Ketones with Arylboronates Bearing Halogen Atoms via C-O Bond Cleavage

While we were investigating ruthenium-catalyzed C-H and C-O arylation reactions with arylboronates, we have found that halogen substituents are tolerated in the coupling reactions. This result suggests that low-valent ruthenium complexes, such as $RuH_2(CO)(PPh_3)_3$, appear to be less reactive for oxidative addition with aryl halides. We applied this unique feature of low-valent ruthenium complexes to synthesis polycyclic aromatic hydrocarbons having halogens on the aromatic rings. Reactions of 1,4- and 1,5-dimethoxyanthraquinones with arylboronates bearing halogen substituents on the aromatic ring were carried out using $RuH_2(CO(PPh_3)_3$ as a catalyst. As we proposed, the arylation took place smoothly to give the desired 1,4- and 1,5-diarylanthraquinones without sacrificing the halogeno groups. This C-O arylation system is useful for synthesizing polycyclic aromatic compounds having quinoidal structures which are expected to have n-type organic field effect transistor properties.

3 Synthesis New n-Type OFET Materials Containing Thiazole Framework

A variety of synthetic methods of PAHs have been developed, so far. Especially, PAHs containing thiophene rings in the molecules are proposed to be attractive for the use of organic semiconductors. In contrast, PAHs involving thiazole rings, instead of thiophenes, have been less explored. We have been investigating applicability of thiazole derivatives as organic field effect transistors. Thiazole derivatives **1** and **2** having carbonyl group bridged framework were chosed as target molecules for our purposes. Compound **1** was synthesized from readily available compound, and its structure was determined by single crystal X-ray analysis which suggests that **1** has planar structure. The measurement of electron mobility revealed that **1** has good electron accepting ability. This result motivated us to study synthesis of further π-conjugated benzothiazole derivative **2** bearing perfluorinated *p*-acetophenone moieties. Compound **2** was obtained in good yield. As expected on the basis of theoretical calculations, we found that **2** has higher electron mobility compared with **1**. These results suggest that PAHs having thiazole frameworks appear promising as OFET materials.

Activation of Stable Small Molecules by Inorganic Metal Clusters

09

Principal Investigator (PI)

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Co-PIs

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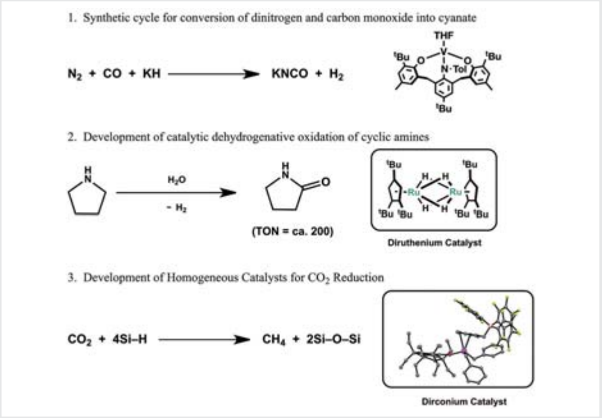
Tsukasa MATSUO
Associate Professor, Kinki University

This research project is intended to establish the method for the construction of the reaction field capable of activation of stable small molecules, involving CO_2, CO and N_2 reduction and C–H/C–C functionalization. Here we utilize metal cluster complexes, in which metal centers can act in concert to engage in substrate binding and to effect multi-electron redox processes. The synergy between these two features on metal cluster complexes could provide a unique strategy for stoichiometric and catalytic transformation of stable small molecules. In this project, we are studying the following subjects.

(1) Synthesis of early transition metal hydride clusters
(2) Synthesis of late transition metal hydride clusters
(3) Activation of stable molecules by hydride clusters
(4) Development of small molecule activation by main group compounds



1 Development of a synthetic cycle for conversion of dinitrogen and carbon monoxide into cyanate

Conversion of atmospheric nitrogen into valuable materials is one of the most challenging problems in chemistry. One approach toward this goal is six-electron reductive N_2 cleavage by soluble transition metal complexes, followed by functionalization of the resulting nitride species and extrusion of N-containing components in subsequent steps. We have developed a vanadium complex having a bis(aryloxide)-anilide tridentate ligand, which is capable of converting N_2 and CO into cyanate in the presence of KH. Treatment of the vanadium complex with KH under an atmosphere of N_2 at room temperature leads formation of a vanadium nitride complex via reductive cleavage of dinitrogen triple bond. Subsequent exposure of the resulting nitride complex to CO at room temperature regenerates the starting vanadium complex with concomitant precipitation of potassium cyanate. Therefore, we complete a synthetic cycle for conversion of N_2, CO, and KH into KNCO and H_2.

2 Development of catalytic dehydrogenative oxidation of cyclic amines

Novel synthetic method for lactams was developed by the use of diruthenium tetrahydrido complex, $Cp^{\ddagger}_2Ru_2(\mu\text{-}H)_4$ $(Cp^{\ddagger} = \eta^5\text{-}C_5{}_tBu_3H_2)$, which contains bulky cyclopentadienyl ligands, $Cp^{\ddagger}$ as a supporting ligand. The diruthenium complex directed dehydrogenative oxidation of cyclic amines by water. Different from the common method for oxidation of amines by using potassium permanganate or iodosylbenzene, this reaction does not require strong oxidants. Thus, this reaction is atom-economical because it produces only dihydrogen as a byproduct. Cooperative interaction of neighboring metal centers of the cluster with substrates, which is important feature of a cluster compound, effectively facilitates the N–H and C–H bond scission of cyclic amines, and provides a cyclic imine ligand on the dinuclear site. The imine intermediate was shown to be a key intermediate, and the imine ligand underwent hydration leading to the formation of lactam.

3 Development of Homogeneous Catalysts for CO_2 Reduction

We have developed new transition metal homogeneous catalysts that enable to convert from carbon dioxide (CO_2) and hydrosilanes to methane (CH_4) and siloxanes under mild conditions (ambient temperature and pressure) with high atom efficiency. The newly developed molecular catalysts possess a highly reactive, coordinatively unsaturated zirconium center supported by a sterically bulky monodentate aryloxide ligand based on the rigid fused-ring 1,1,3,3,5,5,7,7-octa-R-substituted *s*-hydrindacene skeleton. The complete reduction of CO_2 to CH_4 smoothly proceeds under mild conditions, together with the formation of polysiloxanes (silicones), which are the most important organosilicon polymer materials in the silicon chemical industry. We hope that our transformation studies would open a new facet of CO_2 chemical fixation.

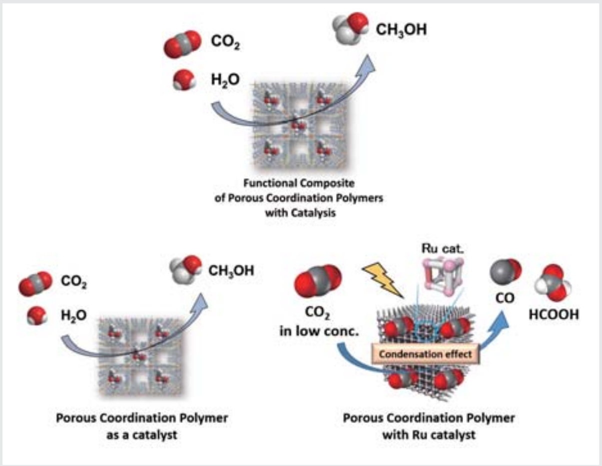
Methanol Synthesis in Porous Coordination Polymers as Reaction Field

10

Principal Investigator (PI)

Susumu KITAGAWA
Director/Professor, Institute for Integrated Cell–Material Sciences,
Kyoto University

Mankind has caused exhaustion of underground resources including oil in exchange of development of advanced civilization. Our project is to develop the catalysis of novel porous coordination polymers (PCPs), which have nanopores, and thus to create new chemistry where methanol is synthesized from carbon dioxide and renewable resources.



1 Water-stable PCPs for Separation of Carbon Dioxide

PCPs are constructed from metal ions/clusters and organic linkers. Because coordination bonds are not very strong, most PCPs are unstable in water and acidic/basic media leading to the collapse of the frameworks. We have synthesized a new PCP having honeycomb-like one-dimensional channels, by using the combination of La^{III} ions and the organic linkers bearing four benzene rings and three carboxylate groups. The PCP is stable both in acidic and basic aqueous media, over a wide range of pH from 2 to 14. In addition, it shows CO_2 separation properties from mixed gases. Although a number of PCPs have been reported to show high ability toward CO_2 separation, this is the first example of PCPs that possess both stability in water and properties of CO_2 separation. These results give an insight into the design of PCP catalysts for methanol synthesis.

2 PCPs for CO_2 Separation from Multicomponent Gas Mixtures

In order to further develop the above-mentioned results, we have designed the organic linker to synthesize a highly stable PCP. We have proposed and validated, experimentally and computationally, a new PCP that has a large aromatic organic surface and show highly separation ability from four-component gas mixtures ($CO_2/N_2/O_2/CO$) at an ambient temperature with low binding energy. Moreover, the PCP shows good water and chemical stability; in particular, it is stable from pH = 2 to 12 at 100 °C, which is unprecedented for carboxylate-based PCPs. In addition, we have also designed and synthesized a family of PCPs constructed by a series of rare earth metals and an organic linker having acylamide functional groups. Among them, only the La^{III}-PCP shows selective capture of CO_2 from ethylene and ethane at high pressure and an ambient temperature, attributed to a unique side-by-side acylamide alignment and structural flexibility. Thus, the strategy of grafting functional groups into flexible PCPs would provide a new type of porous materials for important gas separation.

3 PCP/Molecular Ru complex-Hybrid Catalysts for Reduction of Low Concentrations of CO_2

We have designed and synthesized a new PCP-based hybrid catalyst with a CO_2 reducing Ru^{II} complex incorporated in the form of a metallolinker. The hybrid catalyst adsorbs a larger amount of CO_2, compared with N_2 and Ar, at room temperature. Furthermore, it reacts with an excess amount of hydride to produce methanol, similar to the molecular Ru^{II} complex. Thus, the hybrid catalyst shows both functions originating from the PCP and the Ru^{II} complex. In the photochemical reduction of CO_2, the hybrid catalyst produces two-electron reduction products, CO and HCOOH. The catalytic activity was maintained for all the different content of CO_2 gas, ranging from 100 to 5% CO_2/Ar gas mixture, revealing a synergetic effect between the adsorption and catalytic sites within the PCP hybrid catalyst.

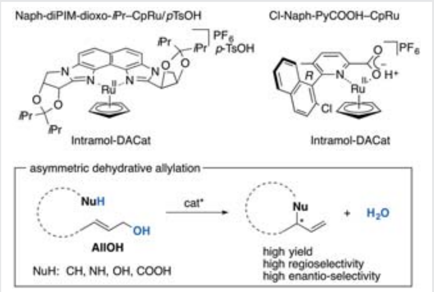
Development of High Performance Transition Metal Catalysts for Dehydrative Asymmetric α-Allylation of Carbonyl Compounds

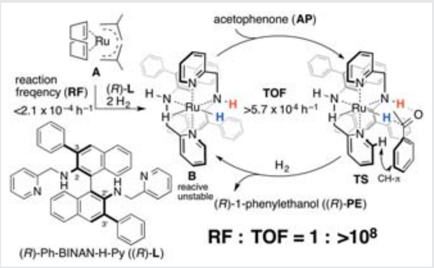
11

Principal Investigator (PI)

Masato KITAMURA
Professor, Graduate School of Pharmaceutical Sciences,
Nagoya University

Coupled with the high synthetic utility of "allyl group," the asymmetric Tsuji-Trost reaction has realized the synthesis of various natural products and has made one of core parts of organic synthesis. Only the disadvantage is, however, that the C–C bond must be formed after enhancing the reaction potential and liberate very stable salt. Ideal is the direct C–C bond formation from protic nucleophiles and allylic alcohols without any stoichiometric activation. Water is only the coproduct. The aim of this project is to develop chiral transition metal complexes realizing such an ideal process as well as new catalytic reactions.





1 Development of Asymmetric Dehydrative Allylation Catalysis

First of all, we have established a catalyst library of transition metal complexes bearing cyclopentadienyl (Cp) group and our new chiral sp^2 nitrogen based bidentate ligand, Naph-diPIM-dioxo-R. The ligand has unique characteristics such as a) high σ electro-donicity, b) near 90° bite angle, c) high rigidity, d) planarity, and e) clear chiral circumstance. Combination of Naph-diPIM-dioxo-R with Cp, which has high electro-donicity, *fac* specificity, and metastability via η^{5}-η^{3}-η^{1} equilibrium, should endow the transition metal complexes with high nucleophilicity and, furthermore, unify the reactive species. Based on our own leading concept "redox-mediated donor-acceptor bifunctional catalyst (RDACat)" or synergetic effect of soft transition metal and hard proton, "acid additive" as well as "transition metal" has been screened, leading to "[Ru(II)Cp(Naph-diPIM-dioxo-*i*Pr)]PF_6/*p*-TsOH **(Cat*)**" combined system. This can catalyze dehydrative allylation of various protonic nucleophiles in high regio- and enantioselective manner. We are currently exploring the applications of this novel catalytic system for asymmetric synthesis and elucidation of detailed reaction mechanisms as well as expansion of the utility of Naph-diPIM-related ligands to other asymmetric catalysis reactions.

2 Catalytic Asymmetric Synthesis of Highly π-Allyl Donative Lactones via Intramolecular Dehydrative Allylation of Carboxylic Acids

Optically active simple lactones with an allyloxycarbonyl moiety (alkenyl lactones) attract much attention from organic synthetic chemists because of their high functional convertibility. Among many excellent catalytic methods, intramolecular Tsuji-Trost (T-T) allylation seems to be the most tangible, but it is limited to only a specific case. We have changed the situation by the reaction of ω-carboxyl-substituted allylic alcohols to the chiral lactones using CpRu(II)/Cl-Naph-PyCOOH catalyst, which is an extention of above catalytic concept (Intermol-DACat) to the intramolecular donor-acceptor bifunctional catalyst (Intramol-DACat). The new method can be applied to the synthesis of various γ- and δ-alkenyl substituted lactones. A detailed analysis of the products obtained from a chirally C(1)-D-labeled substrate has provided a deep insight into the reaction pathway as well as the enantioselection, confirming the Intramol-RDACat mechanism. This success can be ascribed to the higher reactivity of allylic alcohols as compared with the allyl ester products in the present catalysis, which can function under slightly acidic conditions. This new method should further enhance the utility of T-T-type asymmetric allylation, widening the scope of retrosynthetic analyses of natural and unnatural important chiral compounds.

3 Mechanistic Study of the Asymmetric Hydrogenation of Aromatic Ketones Using Ph-BINAN-H-Py–Ru Complexes

Combination of a chiral N4 ligand, (*R*)-Ph-BINAN-H-Py ((*R*)-3,3'-diphenyl-N^{2},$N^{2'}$-bis((pyridin-2-yl)methyl)-1,1'-binaphthyl-2,2'-diamine; **L**), with Ru(π-$CH_2C(CH_3)CH_2)_2$(cod) (**A**) has realized the hydrogenation of acetophenone (**AP**) to (*R*)-1-phenylethanol (**PE**) with a high enantiomer ratio (er), demonstrating the first successful example using non-phosphine-based chiral ligand. The mechanism has been investigated to reveal the unusual aspect: The hydrogenation follows [**PE**] = $k_{obs}t^2$, and an infinitesimal amount of reactive and unstable RuH_2L (**B**) with C_2-Λ-*cis*-α stereochemistry is very slowly and irreversibly generated from **A** by the action of H_2 and **L**, which rapidly catalyzes the hydrogenation of **AP** via our Intramol-DACat mechanism. The time-squared term relates both to the preliminary step before the cycle and to the cycle itself, and the reaction proceeds with a highly unusual eight-order difference in the generation and turnover frequency of **B**. This may be a general tendency in high performance catalysis, but it is too difficult to prove it. The first example has been given by the present study based on detailed kinetic experiments and simulation in combination with various spectroscopic analyses. The results should stimulate our ideas for the molecular catalyst design.

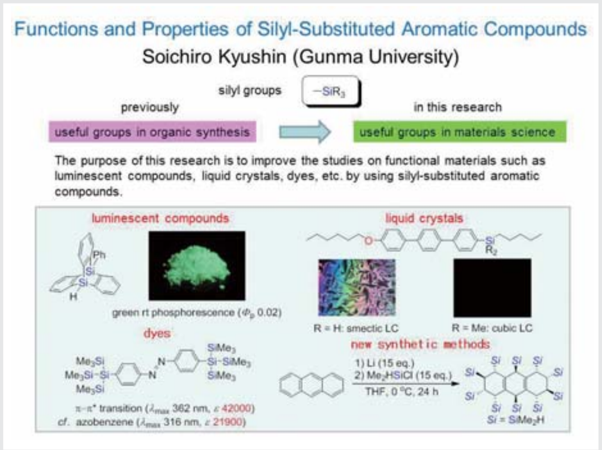
Functions and Properties of Silyl-Substituted Aromatic Compounds

12

Principal Investigator (PI)

Soichiro KYUSHIN
Professor, Graduate School of Science and Technology,
Gunma University

The purpose of this research is to improve the studies on functional materials such as luminescent compounds, liquid crystals, dyes, etc. by using silyl-substituted aromatic compounds. The results obtained in this research are summarized here.



Functions and Properties of Silyl-Substituted Aromatic Compounds

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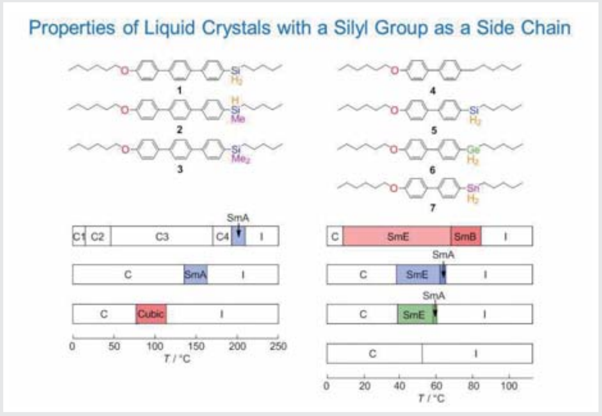


Properties of Liquid Crystals with a Silyl Group as a Side Chain

1 Room-Temperature Phosphorescence of 9-Phenyl-9,10-disilatriptycene

Phosphorescence cannot be usually observed at room temperature but observed in a solid matrix at 77 K to suppress thermal deactivation from the excited triplet state to the ground state. In this research, we found that 9-phenyl-9,10-disilatriptycene shows green room-temperature phosphorescence in a solid state. This compound shows dual fluorescence in a solution at room temperature and intense blue phosphorescence in a matrix at 77 K. These results are in contrast with the fact that its carbon analog shows single fluorescence in a solid state and a solution at room temperature, and in a solid matrix at 77 K. The difference of emission behavior of these compounds, especially the emission mechanism of the room-temperature phosphorescence of 9-phenyl-9,10-disilatriptycene, was explained by theoretical calculations and X-ray crystallographic analysis.

2 Properties of Liquid Crystals with a Silyl Group as a Side Chain

Alkoxy, acyloxy, and alkyl groups have been used as side chains of liquid crystals. In this research, silyl groups were found to be able to be used as side chains of liquid crystals, and their properties have been studied. The silicon atom of a silyl group can be substituted by two groups other than a long alkyl groups. The liquid crystals **1** with two hydrogen atoms and **2** with a hydrogen atom and a methyl group show the SmA phase, but the liquid crystal **3** with two methyl groups shows a cubic phase. In this cubic phase, molecules of **3** form micells, and the micells are packed in a cubic close-packed structure. As a group 14 side chain, a germyl group can be also used. The temperature range of liquid crystalline phases decreases in the order of alkyl (compound **4**) > silyl (compound **5**) > germyl (compound **6**), and the liquid crystalline phase disappears when a stannyl group is used as a side chain (compound **7**).

3 Studies on Silyl-Substituted 5,10,15,20-Tetraphenylporphyrins as Dyes

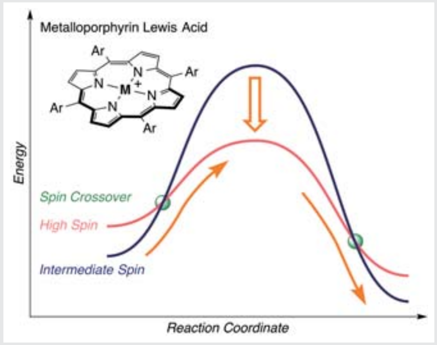
Various silyl-substituted 5,10,15,20-tetraphenylporphyrins have been synthesized, and their photochemical properties have been studied. When 5,10,15,20-tetraphenylporphyrin (TPP) is substituted by silyl groups, no significant change is not observed in the Soret and Q bands of the UV/Vis spectra. However, the quantum yield of singlet oxygen production increases remarkably from 0.58 (TPP) to 0.77 (5,10,15,20-tetrakis(4-trimethylsilylphenyl)porphyrin). Therefore, silyl-substituted 5,10,15,20-tetraphenylporphyrins are potential effective sensitizers for photodynamic therapy of cancers. In fact, after silyl-substituted 5,10,15,20-tetraphenylporphyrins were given to tumor-bearing mice, irradiation to the tumor was carried out to lead to disappearance of the tumor, while 5,10,15,20-tetraphenylporphyrins showed no effect on disappearance of the tumor. This study was carried out as collaboration with Prof. Hiroshi Hiratsuka, the president of Gunma University, Prof. Toshiyuki Takeuchi, a vice-president of Gunma University, Prof. Hiroaki Horiuchi, Graduate School of Science and Technology, Gunma University, and Prof. Masahiro Hosaka, Faculty of Bioresource Sciences, Akita Prefectural University.

Development of Novel Metalloporphyrin Catalyst toward Advanced Catalytic Transformation Program for Carbon Utilization

13

Principal Investigator (PI)

Takuya KURAHASHI
Associate Professor, Graduate School of Engineering,
Kyoto University



The aim of the project is to develop metalloporpyrin catalyst, which would allow us to utilize carbon dioxide as a useful carbon source in organic syhtesis, by focusing attention on unique characters such as spin-state transition and/or mixing of metalloprphyrin complexes. During the course of the study, it was found that the metalloporphyrins could catalyze novel transformations.

1 Diastereoselective Construction of Trans-Fused Octalone Framework via Ruthenium-Porphyrin-Catalyzed Cycloaddition

Octalones are among the most versatile building blocks for the synthesis of various natural products such as polycyclic sesquiterpenes and triterpenes. The [4+2] cycloaddition of cyclohexenones with butadienes, namely, the Diels–Alder reaction, would be one of the most straightforward synthetic routes to octalones with a *cis*-fused framework. This reaction appears to be simple and facile; however, as a matter of fact it is rather difficult to be accomplished due to low reactivity as a dienophile. Hence, the development of efficient catalysts for the reaction remains a research topic of great interest. Efforts have also been devoted to prepare octalones with a *trans*-fused framework by cycloaddition. During the course of our study, we found that the intermolecular reaction of cyclohexenones with 1,3-butadienes affords *trans*-fused octalones in a single step; ruthenium porphyrin was found to catalyze the [4+2] cycloaddition and isomerization at ambient temperature.

2 Iron(III) Porphyrin Catalyzed [4+2] Cycloaddition of Aldehydes with Dienes

Cationic iron(III) porphyrin was found to be an efficient catalyst for the highly chemoselective hetero-Diels–Alder-type reaction of aldehydes with 1,3-dienes. The catalyzed process did not require the use of electron-deficient aldehydes such as glyoxylic acid derivatives or activated electron-rich 1,3-dienes such as Danishefsky's diene and Rawal's diene. The high functional group tolerance and robustness of the catalyst were demonstrated. Further, the potential utility of the catalyst was demonstrated by performing the cycloaddition in the presence of water and by carrying out cycloaddition of an unactivated ketone such as cyclohexanone with a diene.

3 Cobalt Porphyrin-Catalyzed [3+2] Cycloaddition of Cyclopropanes and Carbonyl Compounds

Efficient synthesis of tetrahydrofurans is one of the most important research topics in organic synthesis because they are privileged scaffolds in many natural products and bioactive compounds. Among various synthetic methods, Lewis acid-catalyzed [3 + 2] cycloadditions have emerged as one of the most powerful tools for the synthesis of tetrahydrofurans in the last decades; cycloadditions of malonate-derived cyclopropanes and aldehydes catalyzed by Lewis acids have been reported. We found the cobalt porphyrin-catalyzed regio- and stereoselective intermolecular [3+2] cycloaddition of cyclopropanes with carbonyl compounds. The cycloaddition of cyclopropanes and ketones catalyzed by cobalt porphyrin to afford the corresponding substituted tetrahydrofurans was achieved. The high functional group tolerance and robustness of the catalyst were also demonstrated. Further, the potential utility of the catalyst was demonstrated by performing the cycloaddition of cyclic ketones and cyclopropanes to afford spiro tetrahydrofurans.

4 Ruthenium-Porphyrin-Catalyzed [4+2] Cycloaddition of -Unsaturated Imines and Aldehydes

1,4-Dihydropyridine scaffolds play an essential role in biological processes through NADH regeneration, and show specific and significant medicinal properties, i.e., they function as L-type calcium channel blockers in the treatment of hypertension. Moreover, because of their reducing nature, dihydropyridines have attracted considerable attention as potential biomimetic reductants in combination with organocatalysts. Following Hantzsch's report on the most convenient route to symmetrically substituted dihydropyridines, the medicinal and synthetic applications of these compounds have seen a notable increase. However, for effective control of the chemical properties of dihydropyridines, reliable synthetic routes to *unsymmetrically substituted* or more complicatedly substituted dihydropyridines must be designed. During the course of our study on metalloporphyrin-catalyzed cycloaddition to afford various heterocycles, we found that metalloporphyrins also catalyze the cycloaddition of α,β-unsaturated imines with aldehydes to afford dihydropyridines. We have established a new efficient synthetic route to unsymmetrically substituted dihydropyridine scaffolds via dehydrative [4 + 2] cycloaddition of *N*-tosylated α,β-unsaturated imines with aldehydes in the presence of cationic ruthenium porphyrin catalysts. Variously substituted unsaturated imines and aldehydes can be used for this catalytic system to afford stable *N*-tosyl protected dihydropyridines.

Development and Expansion of Innovative Asymmetric Carbon-Carbon Bond Forming Reactions Based on the Original Basic Sciences

14

Principal Investigator (PI)

Shū KOBAYASHI
Professor, School of Science, The University of Tokyo

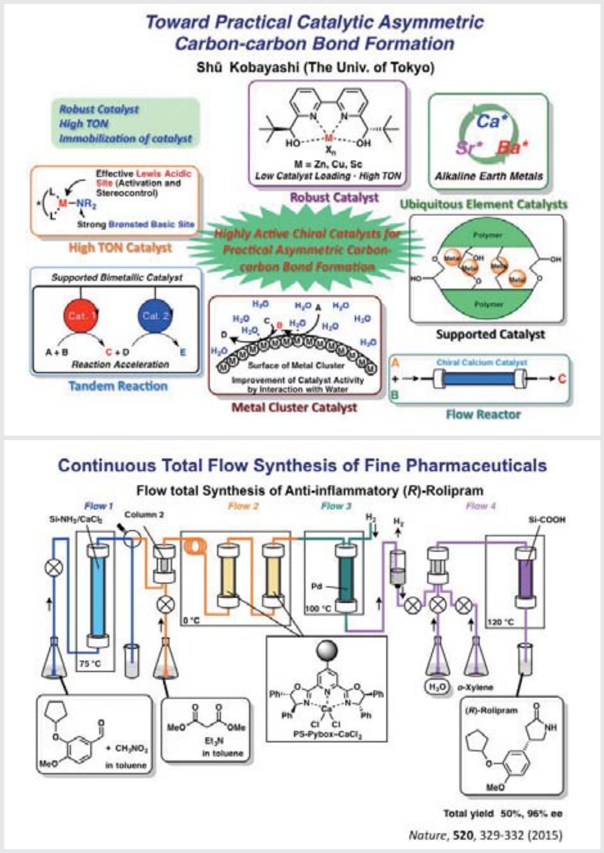
Co-PI

Haruro ISHITANI
Project Associate Professor, School of Science,
The University of Tokyo

The purpose of this project is the development of truly effective chiral catalysts for asymmetric carbon-carbon bond forming reactions, which can be applicable to industrial processes. We will realize highly original technologies by dramatically expanding our own fundamental sciences and collaborating with other related sciences. These researches are aimed towards technological innovations for industrial applications, as well as, revolution of fundamental sciences based on new concepts.

1 Development of catalytic asymmetric direct-type 1,4-addition reactions of simple amides

Carbon–carbon (C–C) bond formation under simple proton transfer conditions is one of the most efficient and frequently employed methodologies in organic synthesis. Recently, a catalytic variant of this reaction, in which an acid/base catalyst works efficiently, has been investigated in detail. However, the applicable pronucleophiles are limited to relatively acidic compounds, and the development of catalytic reactions of weakly acidic carbon pronucleophiles is a challenging research topic. To meet this challenge, we developed a catalytic asymmetric direct-type 1,4-addition reaction of simple amides, which are weakly acidic carbonyl compounds, by using a chiral alkaline metal amide catalyst. The key concept that enabled this catalytic transformation was the formation of strongly basic reaction intermediates. This preliminary result suggests new possibility in base-catalyzed C–C bond forming reactions of weakly acidic carbon pronucleophiles.



Nature, **520**, 329-332 (2015)

2 Development of chiral metal nanoparticle catalysts

Metal nanoparticles show real promise as active catalysts in organic chemistry due to their various interesting properties. However, chiral modification of the nanoparticle surface is normally difficult. Thus, the development of asymmetric catalysis using metal nanoparticles has been recognized to be a challenging topic. Recently, we found that modification of polymer-supported rhodium/silver nanoparticles, by adding a chiral diene, led to an active catalyst for highly enantioselective 1,4-addiiton reactions of arylboronic acids. This discovery should contribute to the evolution of both the chemistry of asymmetric catalysis and the science of metal nanoparticles.

3 Continuous total flow synthesis of fine pharmaceuticals

In industry, multi-steps synthesis of fine chemicals, such as pharmaceuticals, are conducted by performing the various reactions one by one in reaction flasks (batch reaction system). However, the various operations, such as set-up, work-up, and purification of crude product, necessary for each organic reaction requires much time and cost. Therefore, the traditional batch reaction system is time-consuming and not economical. In addition, safety issues of this iterative process can sometimes be problematic. On the other hand, continuous multi-steps flow reaction synthesis using several column reactors, filled with immobilized catalysts, is ideal since it can solve those problems. To demonstrate this, we realized a continuous flow total synthesis of anti-inflammatory drug, (*R*)-Rolipram, using a catalytic asymmetric 1,4-addition reaction by an immobilized chiral calcium catalyst as the key step. This result suggests that multi-step flow synthesis represents the future of manufacturing for supplying fine chemicals and pharmaceuticals in industry.

Development of Supermolecular Catalyst toward CO_2 Reduction System Using H_2O as Electron Source

15

Principal Investigator (PI)

Mio KONDO
Assistant Professor, Institute for Molecular Science

The construction of artificial photosynthetic system, in which CO_2 are reduced by the electrons generated from the oxidation of water, have been attracted considerable attention due to its potential application toward artificial solar energy conversion and storage. Development of molecular catalysts toward water oxidation and CO_2 reduction is considered as serious challenge because it requires multi-electron transfer reaction during the catalysis. Although several molecular catalysts that can catalyze these reactions have been reported, the further improvement of catalytic activity is still required to develop artificial photosynthetic system with the efficiency suitable for practical use. Based on the aforementioned background, in this study, we aim to develop a novel group of supramolecular catalysts which can be applied for artificial photosynthetic reactions in aqueous media(Figure 1).

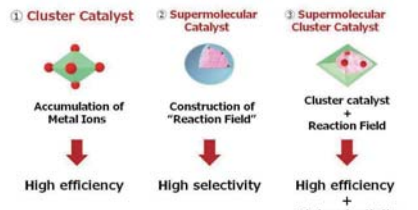


Figure 1

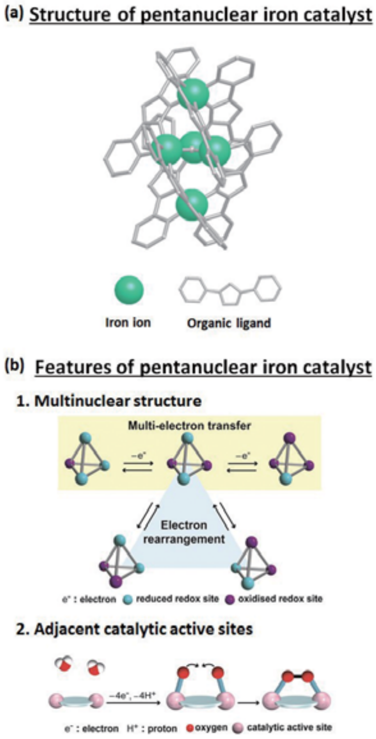


Figure 2

1 Evaluation of activity of a pentairon water oxidation catalyst

One of the important long-standing goals in the field of artificial photosynthesis is the development of efficient and robust water oxidation catalysts based on abundant, inexpensive and environmentally benign metal ions. Iron, the most abundant transition metal element in the earth's crust, is an attractive candidate as a constituent element of water oxidation catalysts. In this study, we focused on a pentairon complex ($Fe_5O(bpp)_6$, bpp =3,5-bis(2-pyridyl)pyrazole, Figure 2), which has multinuclear structure and two adjacent water-activation sites, and evaluated its catalytic activity for water oxidation. Initially, we estimated the turn over frequency (TOF) of the water oxidation reaction from the results of electrochemical measurements. The TOF of $Fe_5O(bpp)_6$ was determined to be 1,900 s^{-1} and was highest among iron-based molecular catalysts reported so far. Moreover, $Fe_5O(bpp)_6$ revealed high selectivity for water oxidation and high robustness (turn over number > 1,000,000) during the catalysis. These results clearly indicate that $Fe_5O(bpp)_6$ is an excellent molecular catalyst for water oxidation.

2 Elucidation of reaction mechanism of water oxidation catalyzed by a pentairon complex

The elucidation of the reaction mechanism of $Fe_5O(bpp)_6$ is highly important to understand the role of its two features: multinuclear structure and two adjacent water-activation sites. Therefore, in this study, we tried to unveil the reaction mechanism based on experimental results and quantum chemical calculations. Several intermediates which form during catalysis were isolated and characterized, and their electronic structures were also determined by several measurements. Furthermore, the thermodynamic parameters of each reaction step were estimated by quantum chemical calculations and the plausible reaction pathways were determined. As a result, we have succeeded to propose the reaction mechanism with high accuracy. In our proposed mechanism, the rapid electron transfer reaction derived from multinuclear structure and the intramolecular O-O bond formation utilizing two adjacent water-activation sites play important role to achieve the efficient water oxidation reaction. These results indicate that the two features of $Fe_5O(bpp)_6$ can provide a breakthrough strategy to obtain efficient water oxidation catalyst based on iron ions.

3 Construction of a water oxidation catalyst with substrate recognition sites

The utilization of the secondary coordination sphere of metal centers is a powerful strategy to design efficient molecular catalyst in chemical conversion processes. Because O-O bond formation by natural photosynthesis is proposed to proceed via the heterometallic reaction between Mn^{V}=O species and Ca^{II}-OH species in the Mn_4CaO_5 cluster, the fabrication of a heterometallic reaction centre in artificial systems should be an interesting and important target. In this study, we have designed a new ruthenium complex bearing $-SO_{3^-}$ groups, where the $-SO_{3^-}$ groups are expected to serve as a functional group to capture Ce^{4+}. The obtained complex showed higher reaction rate compared with the complex without SO_{3^-} groups, indicating that capture of Ce^{4+} ion by $-SO_{3^-}$ and subsequent coordination of water molecule to the captured Ce^{4+} ion forms heterometallic reaction field suitable for intramolecular O-O bond formation. Our findings indicate that the modification of the secondary coordination sphere is an important strategy for the creation of efficient water oxidation catalysts.

Novel Reactions Catalyzed by Metal Clusters Induced by the Ensemble Effect of Multi-Metal System

16

Principal Investigator (PI)

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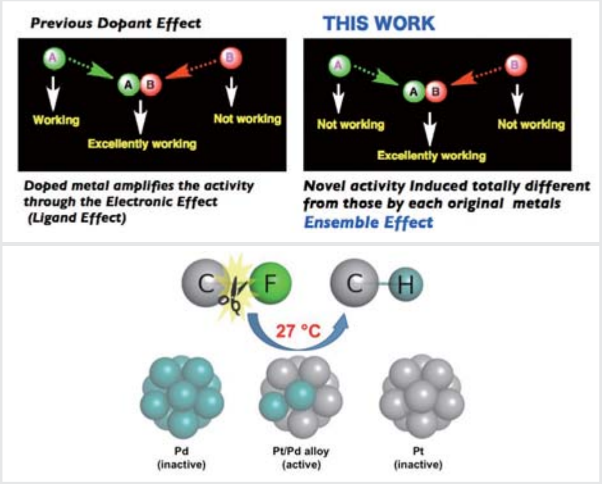
Co-PI

Masahiro EHARA
Professor, Research Center for Computational Science

Recently we found that the bimetallic alloy nanoclusters exhibited totally different catalytic activity from the original monometallic catalysts. These findings strongly suggest us that we have great opportunities to develop the novel reactions, which had never been realized by any types of catalysts, simply through the combination of the metals, as if it were modern alchemy. The objectives of this project involve the development of novel multi-metallic nanoclusters catalysts by the approaches both from experiments and theoretical analyses, to realize novel reactions and energy-saving reactions.



1 Low-temperature Carbon-Chlorine Bond Activation Catalyzed by Gold/Palladium Alloy Nanoclusters

We found that carbon-chlorine bond is activated at low temperature using gold/palladium alloy nanoclusters, which is applied to the effective Ullmann coupling reaction of chloroarene derivatives at room temperature. In general, Ullmann coupling of chloroarenes requires harsh conditions and the corresponding single metal clusters (gold or palladium) do not catalyze the reaction at room temperature. The reaction mechanism is elucidated with the aid of computational chemistry that the adjacent gold and palladium on the surface of the cluster play the indispensable role to activate carbon-chlorine bond by the ensemble effect. In addition, we also clarify the behavior of the palladium nanoclusters catalyst in the coupling reaction by both experimentally and theoretically, which has been discussed for a long time whether the real active species/site is on the surface of the clusters or the leached-out atomic metal. We observed the direct evidence of the atomic metal species participate in the catalytic cycle and the calculation also supports these observations.

2 Carbon-Fluorine Bond Activation at Room Temperature Catalyzed by Platinum/Palladium Alloy Nanoclusters

Our next target is the carbon-fluorine bond activation, which is one of the strongest chemical bond and very few reports have appeared to activate carbon-fluorine bond at low temperature. The carbon-fluorine bond activation is achieved by the combination of palladium and platinum and we develop a new defluorohydrogenation of fluoroarene derivatives at room temperature for the first time. The corresponding reaction cannot be carried out by using single metal clusters such as gold, palladium, or platinum, nor even by gold/palladium alloy clusters, which is successful for the carbon-chlorine bond activation. A series of experiments suggest that the reaction mechanism seems to be totally different from that of gold/palladium-catalyzed carbon-chlorine bond activation as well as other carbon-fluorine bond activation reactions. Finally computational studies elucidates the reaction mechanism involving that each palladium center and platinum center plays independent but cooperative roles in a single catalytic cycle to drastically decrease the energy barrier of carbon-fluorine bond cleavage, which is no more the rate determining step.

3 Polymer Matrix-Induced Activation and Reaction Selectivity in the Catalytic Reaction on the Surface of Metal Nanocluster Catalysts

Nanometer-sized metal clusters are very active catalyst. In other words, the metal clusters should be very reactive species and these are necessary to stabilize to avoid the termination. In our study, organic polymers are used for this purpose because polymers can wrap the clusters to stabilize physically but there is few chemical interaction between the cluster surface and the polymers to keep the active reaction site. Therefore such polymer matrix have been recognized to be inert in the catalytic cycle and no play in the reation except the stabilization. However, recently we found that extremely active gold nanoclusters catalyst can be developed only by changing the combination of the chain length of the polymers and the size of the clusters. The fact strongly suggests us that we have great chance to find novel catalytic activities of the cluster catalysts by tuning the matched morphology and the structures induced by the appropriate polymer design and the clusters. Now we are investigating based on this new concept.

Chemical Immobilization of CO_2 Through Molecular Manipulations of the Crossover and Interfaces between Molecular and Solid Catalyst

17

Principal Investigator (PI)

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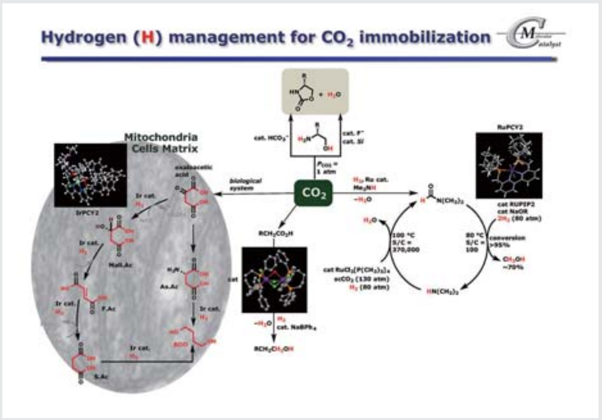
Changeover from the chemical production based on fossil resources to "producing materials from CO_2 and returning to CO_2" would be a foremost consideration in the public society. In this research, chemical manipulations of molecular catalyst and solid photocatalyst and of the crossover and interfaces across these two different catalyst surfaces, at the molecular level, will be carried out for immobilizing CO_2 and CO_2-derivatives as carbon resources. The initial attempt is directed to achieve an advanced method for the conversion of CO_2 to CH_3OH or of carboxylic acids to the corresponding alcohols promoted by catalytic molecular surface (CMS) using heat energy and H_2. Subsequent attempt includes the control of the diversity of hydrogen transfer to CO_2 from CMS that locates around the space nearby or in-between CMS and catalytic solid surface of semiconductor photocataysts, for reduction of CO_2.



1 F– triggers dehydrative reaction of CO_2 with β-aminoalcohols

Catalytic fluoride (F–) is demonstrated to be a trigger for dehydrative immobilization of atmospheric pressure CO_2, such that reaction of CO_2 with β-amino alcohols derived from natural amino acids undergoes dehydrative cyclization via the corresponding carbamic acid intermediates, giving optically pure oxazolidinones in high yields. The reaction was developed based on our recent discovery, in which the dehydrative synthesis of chiral oxazolidinones from CO_2 was catalyzed by HCO_3– (*Tetrahedron Lett.* **2013**). A synergistic combination of fluoride and organosilicon agents (e.g., $Bu_4NF + Ph_3SiF$ or siloxanes) enhances the catalytic activity and functional group compatibility. This system lies at the interface between homogenous and heterogeneous catalysis, and may prove useful for the development of recoverable/reusable siloxane-based CO_2 immobilization materials. This system lies at the interface between homogenous and heterogeneous catalysis, and may prove useful for the development of recoverable/reusable siloxane-based CO_2 immobilization materials (*RSC Adv.* **2014**).

2 Indirect CO_2 transformation to alcohol feedstock: ruthenium carboxylates for self-induced hydrogenation of carboxylic acids

Carbon-neutral alternatives to fossil fuels present a critical challenge for the scientific community in producing a sustainable society. Thus, sourced from biomass and/or as the products of syntheses from CO_2, CAs is a potential renewable resource. We demonstrated that carboxylic acid functions not only as a reactant, but also as an integral part of the "Ru(OCOR)" catalyst (i.e., carboxylic acid self-induced catalysis for carboxylic acid hydrogenation). The hydrogenation proceeded selectively, giving alcohols with functional group tolerance, which has proven challenging with existing heterogeneous/homogeneous catalysts. For example, the high chemoselectivity and concurrent compatibility of aromatic rings and esters (remained unreacted) achieved here is virtually unprecedented, and is rarely possible with typical, strong, stoichiometric agents such as $LiAlH_4$, $LiBH_4$, BH_3, or $LiBEt_3H$ which reduce not only CAs but also esters (*Nat. Commun.* **2015**).

3 Indirect CO_2 transformation to alcohol feedstock: catalytic hydrogenation of C_4-dicarboxylic acids using Ir catalysts

C_4-diarboxylic acids are ubiquitous bio-renewable sources of carbon and richly available as mitochondria metabolites through the TCA (tri-carboxylic acid) cycle (other naming: citric acid cycle or Kelvin cycle) starting with CO_2 immobilization with a pyruvate. We found that (*P,N,N,P*)-Ir complexes catalyzed hydrogenation of succinic acid, fumaric acid, maleic acid, malic acid, aspartic acid, and tartaric acid, convergently giving 1,4-butanediol (BDO) selectively in high yields. Several convergent and stepwise pathways all the way to BDO involve hydrodeoxygenation (HDO), deoxydehydration (DODH), and deamino-deammoniation (DADA). Thus, the nature of Ir complexes resembles that of heterogeneous catalysts, frequently used for HDO and DODH of highly oxygenated compounds such as sugar derivatives under harsh reaction conditions (*PCT patent* **2014**).

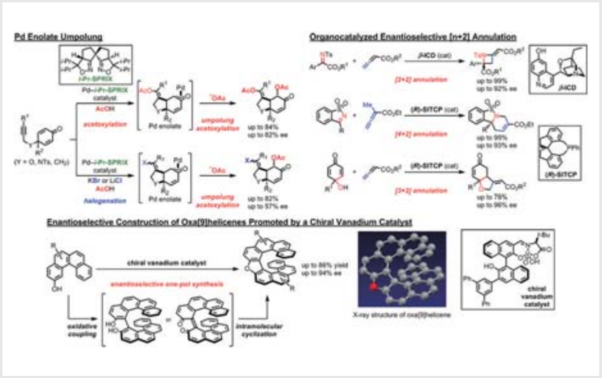
Development of Practical Method for Molecular Transformation Based on Catalytic Asymmetric Domino Reactions

18

Principal Investigator (PI)

Hiroaki SASAI
Professor, The Institute of Scientific and Industrial Research,
Osaka University

The goal of our research project is to achieve an efficient and practical dual catalysis for the synthesis of optically-active pharmaceutically-important compounds, in which the chiral dual catalyst is expected to promote multiple reactions sequentially via independent activation by each of the catalytic sites.



1 Development of Efficient Catalytic Transformation of Carbonyl Compounds Based on Pd Enolate Umpolung

Pd enolates, an analog of π-allyl Pd complexes that one carbon atom of the π-allyl ligand is replaced by an oxygen atom, usually do not exhibit any reactivity toward a nucleophile. Such Pd enolates are known to react with electrophiles, e.g. aldehydes, imines, and enones. Nucleophilic interception of the Pd enolate is therefore promising to be a powerful synthetic method of functionalized carbonyl compounds. We have successfully developed novel Pd-catalyzed reaction involving unusual nucleophilic attack on a Pd enolate using unique SPRIX ligand. Treatment of alkynyl cyclohexadienone substrates with Pd–SPRIX catalyst in acetic acid under an oxygen atmosphere furnished bicyclic products bearing an α-acetoxy carbonyl moiety in good yields. This transformation involved a sequence of the alkyne acetoxylation, the intramolecular cyclization, and the umpolung acetoxylation. Noteworthy is that this cyclative diacetoxylation proceeded enantioselectively in the presence of optically pure SPRIX ligand. Furthermore, cyclative haloacetoxylation of alkynyl cyclohexadienone substrates turned out to occur in the presence of halide source such as KBr and LiCl to give densely functionalized carbonyl products efficiently.

2 Enantioselective Construction of Oxa[9]helicenes Promoted by a Chiral Vanadium Catalyst

Optically active helicenes and other related helical molecules have received considerable attention due to their high potential as catalysts, liquid crystals, and molecular devices. However, efficient enantioselective synthetic method of helicenes, in particular, heterohelicenes, is rather limited. We have previously reported the chiral vanadium-catalyzed oxidative coupling of polycyclic phenols and Friedel–Crafts-type reactions of 2-naphthols with aldimines through chiral Lewis acid catalysis. We envisioned that if the chiral vanadium complexes work as a redox and Lewis acid catalyst for the oxidative coupling of polycyclic phenol, oxa[9]helicene would be obtained in a single operation via oxidative coupling/Lewis acid-mediated intramolecular cyclization sequence. In fact, we found a mononuclear vanadium complex derived from 1,1′-bi-2-naphthol works as a redox and Lewis acid catalyst to promote domino oxidative coupling/intramolecular cyclization of polycyclic phenols to give oxa[9]helicenes in high yields with up to 94% ee.

3 Organocatalyzed Enantioselective [n+2] Annulation

Ketimines are known to be considerably less reactive and unstable than aldimines. Besides, enantioface discrimination of ketimines is more difficult than that of aldimines because of the smaller steric and electronic differences between the two substituents on the prochiral carbon. We have found that a [n+2] annulation of ketimines with allenoates was promoted enantioselectively by an organocatalyst. In a [2+2] annulation of *N*-tosyl α-ketimine esters with allenoates catalyzed by β-ICD, azetidines with a tetrasubstituted stereogenic carbon were obtained in excellent yields with high enantioselectivities. A spiro-type monoaryl phosphine catalyst proved to promote a [4+2] annulation of saccharin-derived ketimines and α-methyl allenoate, which afforded six-membered *N*-heterocycles bearing a tetrasubstituted chiral center in high yields with excellent enantioselectivities. The same spiro-type monoaryl phosphine also catalyzed [3+2] annulation of allenoates and cyclic dienones, which furnished optically active benzofuranone derivatives.

Development of Environmentally-Benign, Waste-Free Dehydrogenative Cross-Coupling Reactions

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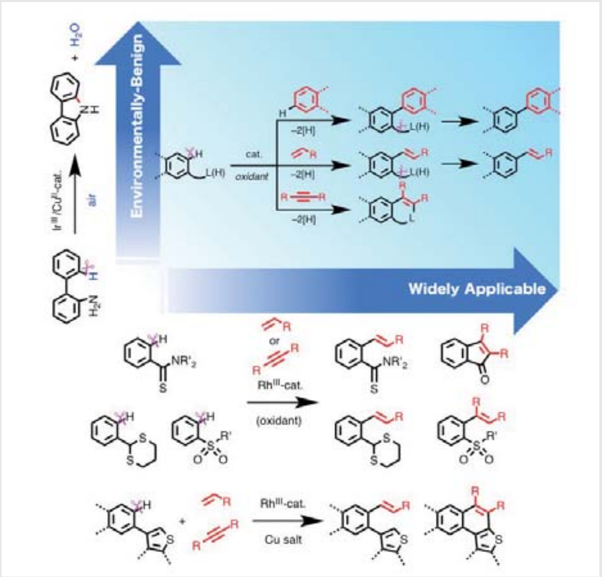
Principal Investigator (PI)

Tetsuya SATOH
Professor, Graduate School of Science, Osaka City University

This project targets the development of environmentally-benign, waste-free dehydrogenative cross-coupling reactions of readily available aromatic substrates with other arenes, heteroarenes, and unsaturated compounds via regioselective C–H bond cleavage. These dehydrogenative coupling procedures provide useful, environment-friendly synthesis routes to various π-conjugated molecules.



1 Development of Dehydrogenative Coupling Reactions Utilizing Sulfur-Containing Directing Groups

One of the most promising C–H bond activation strategies is a chelation assisted version with the aid of a directing group, which leads to regioselective C–H cleavage and functionalization. Oxygen- and nitrogen-containing functional groups are usually employed as directing groups in such transition metal catalyzed C–H direct derivatization reactions. On the other hand, sulfur-containing functional groups are considered to be catalyst poisons because they coordinate metal centers too strongly to suppress the catalytic activities. To our surprise, it was found that sulfur-containing groups such as thioamide-, thioacetal-, and sulfonyl-functions act as good directing groups in rhodium-catalyzed C–H functionalization reactions. Thus, benzothioamides, phenyldithianes, and phenyl sulfones underwent regioselective alkenylation at their ortho positions upon treatment with alkenes or alkynes in the presence of a cationic pentamethylcyclopentadienylrhodium catalyst. These sulfur-containing directing groups seem to be applicable to C–H functionalization reactions using other transition metal catalysts. Related catalytic reactions will be developed.

2 Development of Dehydrogenative Coupling Reactions Utilizing π-Electron Units as Directing Groups

Not only σ-coordinating, heteroatom-containing directing groups but also π-electron units in heteroaromatic substrates were found to induce C–H functionalization at their neighboring positions. For example, treatment of 3-phenylthiophene derivatives with alkenes such as acrylates and styrenes in the presence of a rhodium catalyst and a copper salt oxidant gave ortho-alkenylated products through ortho C–H bond cleavage directed by the π-electron system of thiophene moieties. The dehydrogenative coupling with alkynes proceeded smoothly involving C–H bond cleavages at the 2- and 2′-positions of 3-phenylthiophenes to produce naphthothiophene derivatives. Similar reactions using various phenylthiophenes and –thienothiophenes could be conducted to construct tri-, tetra-, penta-, and hexacyclic frameworks. By using the rhodium catalyst system, 3-phenylbenzofuran and 5-phenylazoles also underwent the dehydrogenative coupling with alkynes utilizing the π-electron systems of furan and azole moieties as directing groups to form benzonaphthofuran and naphthazole derivatives. The annulation procedure provides a straightforward pathway to a variety of fused heteroarene derivatives.

3 Development of Dehydrogenative Cyclization Reactions Using Air as Terminal Oxidant to Synthesize Carbazole Derivatives

It was found that treatment of 2-phenylanilines under air in the presence of an iridium/copper catalyst system induces intramolecular dehydrogenative C–H/N–H coupling to produce the corresponding carbazole derivatives. Coordination of the amino group of the substrates to an iridium center seems to be a key for the regioselective C–H bond cleavage at the 2′-position. A wide range of 2-phenylanilines possessing a variety of substituents are readily available. Therefore, a series of carbazole derivatives possessing various substituents can be easily prepared by this procedure. At the reoxidation step of the iridium catalyst in the catalytic cycle of this reaction, a copper(II) salt is needed. The resulting copper(I) species can also be reoxidized by molecular oxygen in situ under air. Therefore, the amount of the copper salt can be reduced to a catalytic amount. It should be noted that this reaction forms no wastes except for water.

Synthesis of Acrylic Acid Derivatives from Alkenes and CO_2 Using Nickel Catalyst and Development of Novel Type of Immobilized Nickel Catalyst on Gold, SANi (Sulfur-modified Au supported Ni material)

20

Principal Investigator (PI)

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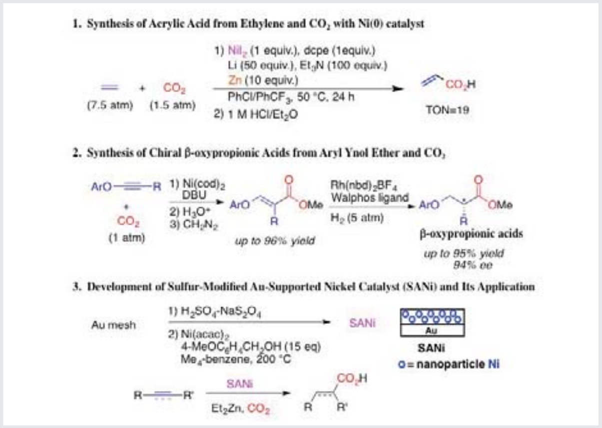
Co-PI

Mitsuhiro ARISAWA
Associate Professor, Graduate School of Pharmaceutical Sciences, Osaka University

Carbon dioxide (CO_2) is an abundant, cheap and relatively non-toxic chemical substance, which should be an ideal C1 unit in synthetic organic chemistry if we could utilize it. Our project focuses a synthesis of acrylic acids via metalalactone formed from multiple bonds (e.g. alkyne, alkene, etc) and CO_2. The preparation of an immobilized Ni(0) catalyst on gold, SANi (Sulfur-modified Au supported Ni material) is also studied with aiming it to utilize in the above-mentioned CO_2 fixation reaction.



1 Synthesis of Acrylic Acid via Nickelalactone formed from Ethylene and CO_2 with Ni(0) catalyst

The synthesis of acrlic acid from ethylene and CO_2 has been extensively studied but still remains as a "dream reaction". We found that the reaction of ethylene (7.5 atm) and CO_2 (1.5 atm) in the presence of NiI_2 (1 equiv.), LiI (50 equiv.), Et_3N (100 equiv.), and Zn (10 equiv.) gave acrlic acid in 1931 % yield besed on Ni complex (TON=19). The reaction conditions and TON are similar with that previously reported by Vogt, but the remarkable improvements are as follows: 1) the pressure of ethylene and CO_2 can be reduced; 2) the use of a large excess amount of Zn can be avoided; 3) a cheaper and stable NiI2 can be used instead of $Ni(cod)_2$.

2 Nickel-Promoted Regioselective Carboxylation of Aryl Ynol Ether and Its Application to the Synthesis of Chiral β-Aryloxypropionic Acid Derivatives

In the reaction of unsymmetrical multiple bonds and CO_2 with metal complex, stereoselective formation of metalalactone intermediate remains still difficult. We found that nickelalactone can be stereoselectively formed from ynol ether and CO_2 in the presence of a nickel(0)-complex, in which carbon-carbon bond formation occurs between the negatively polarized sp carbon atom of ynol and the positive sp carbon atom of CO_2. Hydrolysis of the nickelalactone stereoselectively produced β-aryloxyacrylic acid derivative, which was subsequently subjected to Rh-catalyzed asymmetric hydrogenation, producing corresponding β-aryloxypropionic acid derivative as an optically active form.

3 Development of Sulfur-Modified Au-Supported Nickel Catalyst (SANi) and Its Application

In recent years, supported transition metal nanoparticle catalyst has attracted attention in pursuit of useful and efficient catalyst. Although Pd nanoparticles (NPs) catalysts has been widely investigated and also used in C-C bond forming reactions, the example of other NPs of base metals such as Ni are still limited. We have recently developed a sulfur-modified Au-supported Pd catalyst (SAPd) that is a very practical immobilized palladium catalyst for various reactions such as Suzuki-Miyaura coupling. In this project, we recently succeded in developing a sulfur-modified Au-supported Ni catalyst (SANi) using a combination of the immobilization method employed for preparation of SAPd and an appropriate reducing agent. Thus, SANi was prepared by treatment of sulfur-modified Au mesh with $Ni(acac)_2$ as a Ni source and 4-methoxybenzyl alcohol as a reductant in Me_4-benzene at 200 °C. The Ni-K edge X-ray absorption fine structure of SANi revealed that the Ni(0) NPs (ca. 3 nm) were immobilized on support. Furthermore, we found that SANi could apply to various cross coupling reactions as well as hydrocarboxylation reaction of alkyne and alkene with CO_2.

Development of Asymmetric C–H Bond Activation Catalysts Guided by Quantum Simulations

21

Principal Investigator (PI)

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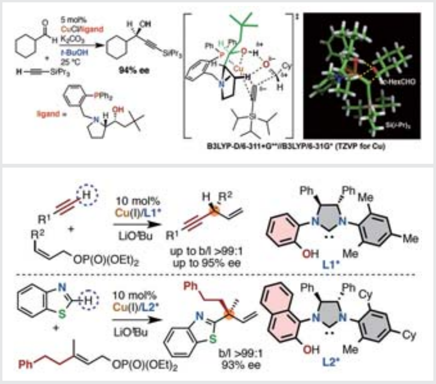
Professor, Hokkaido University

Co-PIs

Seiji MORI
Professor, Ibaraki University

Tetsuya TAKETSUGU
Professor, Hokkaido University

This project aims at developing high-performing chiral transition metal catalysts that realize selective transformations of carbon–hydrogen bonds for streamlining synthetic processes. Our unique strategy for achieving this challenging goal is to take full advantage of quantum mechanical simulations prior to experiments. Brand-new automatic reaction pathway exploration methods such as "artificial force induced reaction (AFIR) method" are used to conduct quantum mechanical simulations for gaining mechanistic understanding of the reactions developed in this program and for assisting the design of new catalysts and reactions. Development of new quantum mechanical simulation methods is also important subject of this project.



1 Development of Borylation Reaction of Unactivated sp^3-C–H Bonds Using Solid-supported Monophosphine-Metal Systems

Under the influence of a Ir catalyst with solid-supported cage-type phosphine Silica-SMAP, borylation of sp^3-C–H bonds in simple alkyl groups, which have neither electronically activating group nor unsaturated bond, occurred regioselectively with the assistance of a coordination-driven directing effect of a pyridyl group. This catalysis is effective even for the reaction of secondary C–H bonds, affording secondary alkylboronates in high yields under mild conditions. Heteroaromatic rings other than pyridine and imine derivatives also work as effective directing groups. Borylation of sp^3-C–H bonds in cyclopropanes and cyclobutanes appeared to be particularly reactive: even tertiary sp^3-C–H bonds participated in the borylation.

2 Construction of Hydrogen-bonding-copper(I) Cooperative Catalyst Systems and Development of Enantioselective Reactions Based on Activation of sp-C–H Bonds of Terminal Alkynes

The hydrogen-bonding-copper(I) cooperative catalyst systems have been prepared from copper(I) salts and chiral ligand that was constructed through covalent connection between triphenylphosphine derivatives and chiral aminoalcohols. These systems allowed the highly enantioselective alkynylation of aldehydes with terminal alkynes to afford enantioenriched secondary propargylic alcohols, which are versatile intermediates for the synthesis of chiral compounds. DFT analysis of reaction pathways revealed that ligand–substrate hydrogen-bondings occur in alcoholic solvents and that a non-classical hydrogen bond donated by a non-polar sp^3-C–H bond in the chiral ligand play an important role for the enantioselection.

3 Construction of Phenol-NHC-Cu(I) Chiral Catalyst Systems and Development of Enantioselective Allylation of Terminal Alkyne/Azole Pronucleophiles

We developed copper-catalyzed enantioselective allylic alkylation of terminal alkynes. High enatioselectivity was achieved by employing a chiral *N*-heterocyclic carbene ligand containing a phenolic *N*-substituent. Various terminal alkynes can directly be used without pre-activation of their sp-C–H bonds. More recently, we succeeded in constructing quaternary stereogenic centers through the enantioselective allylation of sp^2-C–H bonds of azole derivatives.

4 Expansion and Speeding-up of Automated Search of Reaction Pathways by Quantum Chemical Calculations

We have advanced the development of "Artificial Force Induced Reaction (AFIR) method", which is our original tool for automated search of reaction pathways (Maeda, S.; Morokuma, K. *J. Chem. Phys.* **2010**, *132*, 241102). Specifically, the AFIR method, which had been developed only for searching intermolecular reaction pathways (multi-component AFIR: MC-AFIR), has been extended so that it can treat intramolecular reactions such as isomerization and decomposition (single-component AFIR: SC-AFIR). This has allowed systematic analysis of isomerization and decomposition of catalyst intermediates. Moreover, we combined the AFIR methods and QM/MM methods in order to analyze asymmetric metal-catalyzed reactions for their reaction pathways and mechanism of enantiocontrol. Through this research, we confirmed applicability of the AFIR methods for the research of C–H activation catalysis and asymmetric catalysis. This research also revealed some limitations and problems of the methods. Improvement of calculation programs for solving these problems is ongoing.

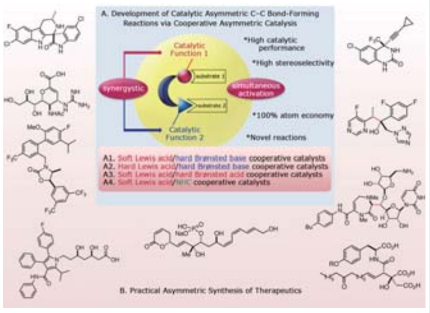
Development of Advanced Practical Cooperative Asymmetric Catalysts and Their Application to Streamlining Enantioselective Synthesis of Therapeutics

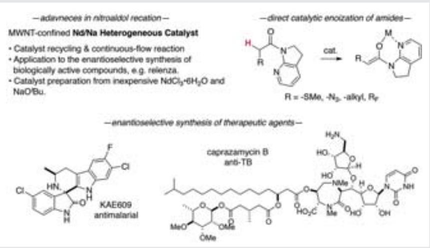
22

Principal Investigator (PI)

Masakatsu SHIBASAKI
Director, Institute of Microbial Chemistry, Tokyo

Given the global situation in logical drug design and development, a reliable, robust, and practical methodology that enables the efficient production of chiral compounds is urgently required. In this project, we are developing a series of cooperative catalysts exhibiting multiple catalytic functions that promote specific enantioselective C–C bond-forming reactions with perfect atom economy. These reactions will streamline the enantioselective synthesis of therapeutics with minimal undesired by-products.





1 Development of heterogeneous Nd/Na asymmetric catalyst confined in carbon nanotubes

We developed a Nd/Na/amide-based ligand catalyst confined in multi-walled carbon nanotube (MWNT) network. Self-assembly of the catalyst proceeded in the matrix of MWNT, resulting in a solid catalyst that exhibited high catalytic performance in *anti*-selective asymmetric nitroaldol reaction. This solid catalyst allowed for repetitive use after the reaction and could be applied to the reaction in a continuous-flow platform with high turn-over number. Stereoselective nitroaldol reactions provide synthetically versatile enantioenriched 1,2-amino alcohols, which find broad utility in enantioselective synthesis of biologically active compounds. Indeed, this catalysis was applied to the enantioselective synthesis of relenza, a clinically used anti-influenza drug. $NdCl_3 \cdot 6H_2O$ can be used as an inexpensive and abundant Nd source for prospective large-scale application.

2 Catalytic asymmetric C–C bond forming reactions via in situ generated amide enolates

Enolates play a central role for asymmetric C–C bond forming reactions in organic synthesis. From late 90's, "direct" use of carbonyl compounds as enolate precursors have attracted growing attention as a more advanced methodology in terms of both atom and step economy; the direct and catalytic enolization of carbonyl compounds obviated the use of stoichiometric reagents and a separate operation for enolate formation. However, ease of direct enolization is highly dependent on the acidity of carbonyl compounds, and the least acidic amides have rarely utilized in direct enolization chemistry. We designed a 7-azaindoline amide substrate that can be specifically activated by soft Lewis acid/Brønsted base cooperative catalyst, enabling facilitated enolization and subsequent enantioselective addition to electrophiles e.g. aldehydes (aldol reaction) and imines (Mannich reaction). MeS-, N_3-, alkyl-, fluoroalkyl-substituents can be introduced to α-position of the amides, producing various aldol and Mannich adducts bearing variety of α-substituents. The activation mode of 7-azaindoline amide is also valid for electrophilic activation; α,β-unsaturated amide is known as almost unreactive Michael acceptor, but α,β-unsaturated 7-azaindoline amides exhibited high reactivity with the cooperative catalyst to afford corresponding Micheal adducts with high stereoselectivity.

3 Total synthesis of biologically active compounds by using cooperative asymmetric catalysts

We are particularly intrigued by the development of catalytic asymmetric C–C bond forming reactions because these reactions provide the most efficient synthetic methodology of enantioenriched chiral building blocks of interest. Synthetic studies of biologically active compounds that can contribute to the human society are a suitable playground to evaluate the practical utility of these catalysts. Recently, we have completed the enantioselective total synthesis of KAE609 and caprazamycin B, an anti-malarial drug candidate and a highly active compound against multi-drug resistant mycobacterium tuberculosis strains, respectively. In the synthesis KAE609, direct catalytic asymmetric alkynylation of ketimines played a pivotal role for the construction of the requisite tetrasubstituted stereogenic center. Ketimines have refused challenges of a number of catalysts due to their low reactivity and difficulty in prochiral face selection, and the use of cooperative catalysis was key to make the direct asymmetric addition proceed smoothly. For structurally complex caprazamycin B, three catalytic asymmetric reactions, direct aldol reaction of thioamides, nitroaldol reaction, and desymmetrization, were utilized to construct carbon frameworks with concomitant control of stereochemistry. These examples highlight the synthetic utility of cooperative asymmetric catalysts in practical synthetic chemistry.

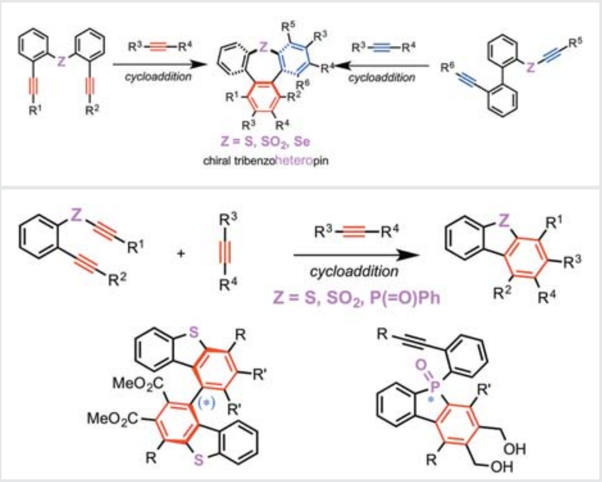
Construction of Chiral p Space by Using Transition Metal-Catalyzed Asymmetric Reactions and its Application to the Functional Materials

23

Principal Investigator (PI)

Takanori SHIBATA
Professor, Waseda University

My research project is a new design and synthesis of 3D molecules containing aromatic rings, especially heteroaromatic ring, using transition metal-catalyzed asymmetric reactions. In particular, I focus on the creation of "chiral space" which is constructed by either right-handed or left-handed moiety. My final goal is the development of new physical properties derived from the chiral 3D space constructed by (hetero)aromatic π-electron system.



1 "Enantioselective Synthesis of Chiral Multi-Substituted Tribenzoheteropins by the Catalytic Cycloaddition"

Tribenzoheteropin is an *ortho*-benzannulated seven-membered heterocycle possessing an 8π electron system with a heteroatom. There has been only an example of catalytic synthesis and no report of the enantioselective synthesis. We achieved the first catalytic and enantioselective synthesis of multi-substituted tribenzoheteropin derivatives. The chiral rhodium-catalyzed reaction using diphenyl sulfide-tethered diynes and 2-phenyl sulfanylbenzene-tethered diynes with a monoalkyne gave chiral multi-substituted tribenzothiepins having different types of substitutions respectively in good to excellent ee under the mild conditions. The present protocol could also be used for the preparation of a chiral tribenzothiepin dioxide and tribenzoselenepin.

We further calculated the inversion energy of these saddle-shaped molecules by measurement of the racemization rate using the Eyring kinetic equation under heating conditions. I will discuss on the different energy dependent on the substitution patterns and hetero atoms.

2 "Multi-Substituted Dibenzothiophen and Dibenzophosphole Oxide Synthesis by the Catalytic Cycloaddition"

Dibenzothiophen (DBT) and dibenzophosphole oxide (DBP) are important skeletons in organic chemistry because they are found in many organic electronics and materials. Therefore, many approaches to them have been reported, but the catalytic protocol for the synthesis of multi-substituted compounds is still limited.

We developed an approach using Rh-catalyzed [2+2+2] cycloaddition, which is reliable and atom-economical for the construction of multicyclic six-membered ring systems. The sulfanylbenzene-tethered and phosphorylbenzene-tethered 1,6-diynes with alkynes gave various multi-substituted DTP and DBP derivatives under relatively mild reaction conditions. In addition, highly enantioselective synthesis of an axially chiral 1,1′-bi(dibenzothiophenyl) and a P-chiral dibenzophosphole oxide derivative was achieved.

3 "Enantioselective Synthesis of Planar-Chiral Benzosiloloferrocenes by Rh-Catalyzed Si-H/C-H Coupling"

Dibenzosilole is an important skeleton of many functional molecules that are useful as conjugated organosilicon materials in organic electronics and photonics. Ferrocene is also an important core of many organometallic compounds that attract much attention in medicinal chemistry and material science. We merged them together and created a new class of planar-chiral compounds "benzosiloloferrocenes".

We achieved the asymmetric synthesis of them by enantioselective "cross dehydrogenative coupling" of an sp^2 C-H bond of ferrocene with a Si-H bond. The enantioselective synthesis of planar-chiral ferrocenes by C-H bond activation is a hot topic in these years, and the present transformation is the first example via cross dehydrogenative coupling.

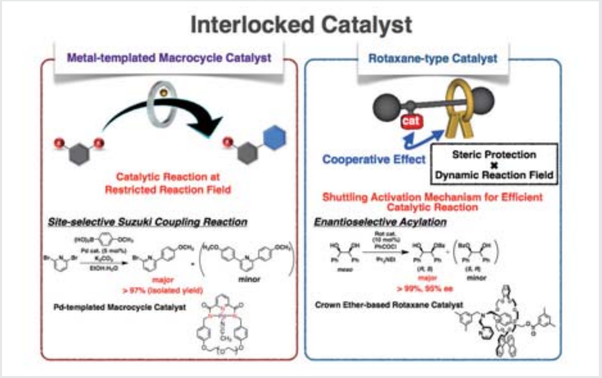
Highly Selective Efficient Transformation of Polymers Exploiting Interlocked Catalyst

24

Principal Investigator (PI)

Toshikazu TAKATA
Professor, Department of Chemical Science and Engineering,
Tokyo Institute of Technology

The present research objective is to develop "interlocked catalyst" that consists of a macrocycle catalyst exhibiting its catalytic function via the formation of the pseudorotaxane-type intermediate. According to its characteristic, application of the interlocked catalyst to polymer substrate resulted in the remarkably accelerated reaction via the promotion of successive reactions based on the proximity effect originating from the topological structure of the intermediate pseudorotaxane. The interlocked catalyst system was believed to open up new insight for the effective polymer reaction. In addition, the development of novel catalyst systems capable of attaining both the size- and shape-selective molecular transformations is also one of the research purposes.



1 Synthesis of novel macrocycle catalyst

The synthesis of novel macrocycle catalyst is essential for the development of interlocked catalyst system. However, only a few reports of the synthesis of macrocycle ligands bearing enough cavity size to encapsulate the guest molecules have been reported. In addition, the relationship between the cavity size of macrocycle catalyst and its catalytic activity was unclear. We have been successfully synthesized several macrocycle ligands consisting of different coordination sites, and developed efficient synthetic approach to obtain macrocycles with different cavity size. The Pd, Cu, Ru, and Pt-templated macrocycle catalysts were synthesized and their structures were studied so far. These macrocycle catalysts have a potential to exhibit unique catalytic activity and to construct novel catalytic systems.

2 Highly efficient catalytic conversion utilizing Pd-tethering interlocked catalyst

The effective intramolecular hydroamination reaction of allyurethanes including polyallylurethanes via an intermediary pseudorotaxane formation was achieved using a Pd-tethering macrocycle catalyst. The highly accelerated polymer reaction could proceed as a result of the dramatic change of the association constant between the macrocycle catalyst and substrate or product before and after the reaction, leading to successive wheel translation along the reactive sites on the polymer axle. While the reactions of low molecular weight substrates at the initial stage in the presence of the macrocycle catalyst was faster than those of high molecular weight substrates, the relation was inverted at the latter stages. In addition, the reaction rate of high molecular weight substrates was almost constant, or even accelerated in the latter period. When an acyclic catalyst was employed under the same reaction conditions, no such unique behavior was observed. These results suggest that the reaction of high molecular weight substrates proceed independent on the concentration of the remaining reaction sites, probably due to the proximity effect originating from the topological structure of the pseudorotaxnae intermediate with the macrocycle catalyst. We then elucidated high generality of polymer substrates which can undergo this unique reaction even by changing the polymer structures.

3 Site-selective Suzuki coupling reaction utilizing Pd-templated interlocked catalysts

In general, it is difficult to catalyze only one specific site from several equally reactive sites. On the contrary, we have developed site-selective Suzuki coupling reaction with Pd-templated macrocycle catalyst. The coupling reaction of 2,6-dibromopyridine with excess amount of boronic acid was carried out to give monoaryl bromopyridine in high yield. In addition, the site-selectivity was enhanced as the cavity size of macrocycle ligands got smaller. There are distinct relationship between the cavity size of macrocycle catalyst and its activity. The one-pot synthesis of unsymmetric diarylpyridine was achieved in excellent yield with this catalyst. As the site-selectivity were observed with the use of various boronic acids in this catalytic system, the easy synthesis of a wide variety of unsymmetric substrates are expected to

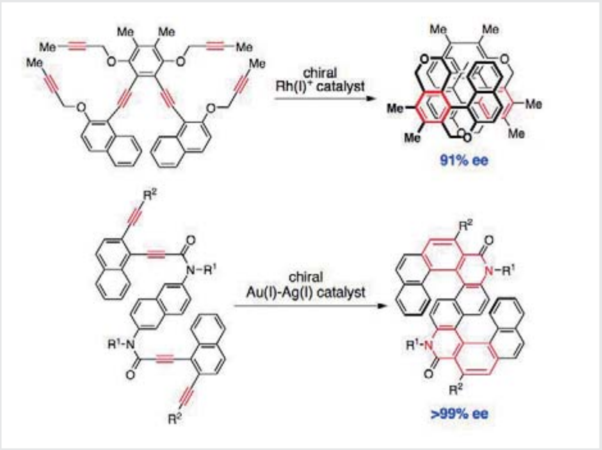
Advancement and Application of Catalytic Ring Construction by Asymmetric Carbon–Carbon Bond Forming Reactions

25

Principal Investigator (PI)

Ken TANAKA
Professor, Department of Chemical Science and Engineering,
Tokyo Institute of Technology

In this research, as a novel method for the synthesis of aromatic compounds based on a new concept in place of the cross-coupling reactions, we will establish the method, which is able to assemble aromatic compounds from already functionalized small organic compounds.



1 Construction of Non-centro- and Centro-chiralities by Cationic Rhodium(I) Complex-Catalyzed [2+2+2] Cycloaddition

Our research group achieved the asymmetric synthesis of axially chiral biaryls and planar chiral cyclophanes by the cationic rhodium(I) complex-catalyzed chemo-, regio-, and enantioselective [2+2+2] cycloaddition of alkynes. In addition, in order to create the novel organic molecules showing good optical and chiroptycal properties, we have achieved the enantioselective synthesis of the higher-order helicenes by the cationic rhodium(I) complex-catalyzed chemo-, regio-, and enantioselective [2+2+2] cycloaddition of alkynes. We have also achieved the synthesis of a symmetrically multi-functionalized [12]cycloparaphenylene by the cationic rhodium(I) complex-catalyzed chemo- and regioselective intermolecular [2+2+2] cycloaddition of alkynes. Not only the construction of non-centrochiralities but also that of multiple centro-chiralities have been achieved by the chemo-, regio-, and enantioselective [2+2+2] cycloaddition involving alkenes or carbonyl compounds.

2 Heterocycle Synthesis by Electron-Deficient Cationic Rhodium(III) Complex-Catalyzed C-H Bond Activation

On the other hand, our research group reported the synthesis of an ethoxycarbonyl-substituted cyclopentadienenyl rhodium(III) complex [Cp^ERhCl_2]. In situ generated electron-deficient dicationic rhodium(III)/Cp^E complex, derived from Cp^ERhCl_2, showed higher catalytic activity than the dicationic rhodium(III)/Cp* complexes in the C–H bond functionalization of electron-rich arenes to produce various heterocycle under ambient conditions. For example, this rhodium(III) catalyst is a highly active precatalyst for the oxidative annulations of anilides and benzyl alcohols with both activated and unactivated alkynes under ambient conditions (at room temperature under air). The oxidative sp^2 C-H bond olefination of anilides with both activated and unactivated alkenes is also catalyzed by this rhodium(III) catalyst under ambient conditions. Furthermore, this rhodium(III) catalyst is able to catalyze the oxidative double annulation of anilides with two alkynoates under ambient condition.

3 Heterocycle Synthesis by Cationic Gold(I)-Silver(I) Complex-Catalyzed Alkyne π-Bond Activation

Our research group established that the cationic gold(I)-silver(I) complex bearing a axially chiral biaryl bisphosphine ligand is able to catalyze the asymmetric quadruple intramolecular hydroarylation reactions to produce helically chiral higher-order azahelicenes with high yields and enantioselectivity. For example, the enantioselective synthesis of S-shaped double azahelicenes has been achieved via the gold(I)-silver(I) complex-catalyzed sequential intramolecular hydroarylation of alkynes. The use of excess AgOTf toward a gold(I) complex is crucial for this transformation. Interestingly, the circularly polarized luminescence activity of the S-shaped double azahelicenes was significantly higher than that of the azahelicenes. In addition, the enantioselective synthesis of an aza[10]helicene, possessing two pyridone units, has been achieved via the gold(I)-silver(I) complex-catalyzed intramolecular quadruple hydroarylation of a tetrayne. This aza[10]helicene was successfully converted into a fully aromatic aza[10]helicene, possessing two pyridine units. Structure-photophysical and chiroptical properties relationship in a series of azahelicene isomers has also been examined, which revealed that the S-shape in helicenes increases the quantum yields and anisotropy factors, but decreases the optical rotation values.

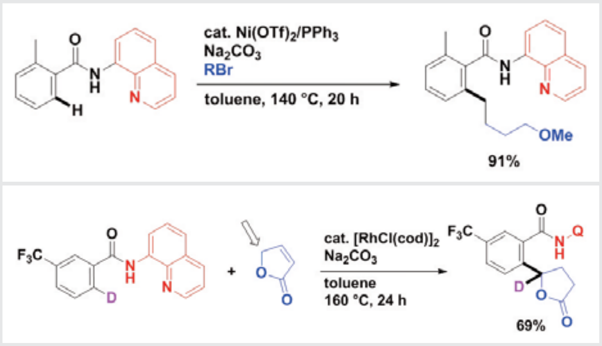
Development of New Methodology for Environmentally Friendly Transformation

26

Principal Investigator (PI)

Naoto CHATANI
Professor, Osaka University

The functionalization of C-H bonds, the most common bond found in organic compounds, represents one of the most important environmentally friendly and efficient synthetic methods, provided it could be accomplished without the need for additional intermediate steps. The aim of this project is to develop a breakthrough methodology that will permit the catalytic activation of C-H bonds and to develop straightforward synthetic transformations of such bonds. A final goal is to develop a catalytic transformation of C-H bonds that would be superior to the currently used cross-coupling reactions. Our plans include the development of new catalytic reactions by taking advantage of chelation assistance in conjunction with *N,N*-bidentate directing groups.



1 Ni(II)-Catalyzed Functionalization of C-H Bonds

The use of low cost and more abundant metals, especially nickel complexes, has attracted considerable recent attention for use in the functionalization of C-H bonds. However, most of the Ni-catalyzed functionalization of C-H bonds reported to date involve C(sp^2)-H bonds in specific aromatic systems that contain acidic C-H bonds. In a previous study, in 2013, we reported on the Ni(II)-catalyzed alkylation of C-H bonds in aromatic amides consisting of an 8-aminoquinoline group with alkyl halides. We also further examined arylation, methylation, benzylation, sulfonylation, and iodination reactions in such systems. The system is also applicable to, not only C(sp^2)-H bonds, but also C(sp^3)-H bonds. A combination of Ni(II) catalysts and an 8-aminoqunoline directing group is now recognized as a powerful system for the Ni(II)-catalyzed chelation-assisted activation of C-H bonds and a number of Ni(II)-catalyzed transformations of C-H bonds using this protocol has been also reported by other groups.

2 Rh(I)-Catalyzed Functionalization of C-H Bonds

An unprecedented C-H alkylation using α,β-unsaturated γ-lactones and dihydrofurans was achieved by the Rh(I)-catalyzed reaction of aromatic amides. C-C Bond formation occurs between the ortho-position in the benzamide derivatives and the γ-position of the α,β-unsaturated γ-lactones. The presence of an 8-aminoquinoline directing group is crucial for the success of the reaction. The results of deuterium labeling experiments suggest that a migratory carbene insertion is involved as the key step in the catalysis. A similar type of the reaction was also achieved using styrenes and α,β-unsaturated acyclic carbonyl compounds as the alkene.

3 Ru(II)-Catalyzed Functionalization of C-H Bonds

Alkylation of C-H bonds with α,β-unsaturated ketones was achieved by the Ru(II)-catalyzed reaction of aromatic amides. Although the oxidative alkenylation of C-H bonds with α,β-unsaturated carbonyl compounds is well known, only limited examples of the alkylation of C-H with α,β-unsaturated carbonyl compounds bonds are available. This reaction is the first example of the application of methyl vinyl ketone, which is easily polymerized, to C-H functionalization reactions. Furthermore, the arylation of C-H bonds in aromatic amides with aryl iodides was also achieved in the presence of a Ru(II) catalyst. In both reactions, the presence of an 8-aminoquinoline directing group is crucial for the success of the reaction

Novel C1 Chemistry Process to Convert Carbon Dioxide

27

Principal Investigator (PI)

Noritatsu TSUBAKI
Professor, Graduate School of Engineering,
University of Toyama

Carbon dioxide reacts with methane (natural gas or shell gas) and air (oxygen) to form syngas which is the mixture of carbon monoxide and hydrogen, without the heat provided. And then the obtained syngas can be catalytically converted efficiently to methanol, dimethyl ether, and ethanol by our new synthesis routes and new-concept catalysts (Figure 1). 1, Effective synthesis of syngas (mixture of carbon monoxide and hydrogen) from comprehensive catalytic reforming of methane, carbon dioxide and oxygen/air is conducted using new catalysts with the optimized nano-structure and tailor-made, new catalytic material. 2. Methanol and DME (Dimethyl Ether) synthesis at low temperature using syngas from 1 and carbon dioxide is accomplished by a new low-temperature route invented by us. 3. Ethanol synthesis from DME from 2 and syngas from 1 is realized by a new reaction route proposed by us, by developing new-concept powerful catalyst.

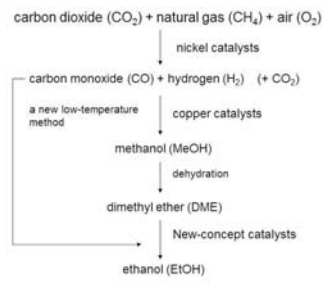


Fig. 1 Reaction target scheme of the present research

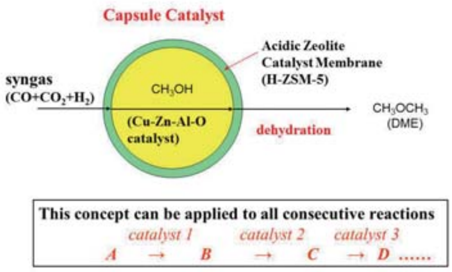


Fig. 2 Concept of capsule catalyst and its application for one-step synthesis of dimethyl ether (DME)

1 Production of syngas from CO_2, CH_4 and O_2 (air) by auto-thermal reforming catalysis

For 1 above, energy from outside is not necessary to be provided. A part of methane can be combusted to provide heat in situ, as an auto-reforming mode. Other methane is reformed with the co-fed carbon dioxide and the carbon dioxide in situ formed as well as steam in situ formed, to provide syngas with a suitable H_2/CO ratio at 1-2. New type Ni-based catalyst or Ni catalyst added by the second metal promoter is developed to fulfill this reaction with very high rate such as 30000-50000 h^{-1} GHSV. On the details of syngas production from $CO_2+CH_4+O_2$, the endothermic reaction of CO_2+CH_4 reforming is coupled with the exothermal reaction of $CH_4+0.5O_2$ partial oxidation, using quick heat transfer property of the SiC catalyst, to realizing high heat efficiency of this comprehensive methane reforming. Ni supported on SiC catalyst support exhibits excellect activity, lifetime and promoter effects.

2 New low-temperature synthesis method of methanol and dimethyl ether (DME)

For 2 above, methanol and DME can be quickly obtained at high one-pass conversion, without thermodynamic equilibrium limitation, via ester intermediate. This new route is invented by us (N. Tsubaki, Acc. Chem. Res., Vol. 46, 1838, 2013). Various catalysts, reactors, catalytic solvents are investigated in detail to pursue the enhanced activity and selectivity. Especially a lot of active Cu-ZnO-based catalysts are prepared by the latest nano science methods accompanied by concrete characterization. At low temperature such as 443K and low temperature such as 30bar, only half of the conditions of the present commercial plant, our catalyst and new method reach STY of 500-1300 g-MeOH/kg-cat.h (without recycle of the unreacted gas), extremely higher than the STY of 400 g-MeOH/kg-cat.h of the present commercial plant (with recycle of the unreacted gas), because our one-pass conversion is as high as 90%-100%, remarkably higher than the conversion of 14%-20% in ICI commercial plant. Industrial production scale-up is also now under preparation.

3 New ethanol synthesis method from DME and syngas

For 3, ethanol is selectively, efficiently produced from DME and syngas by a new reaction route invented by us, using powerful new-concept catalyst developed by us (ChemSusChem, hot paper). Recently, we developed a nano-sheet-like catalyst to accelerate the reaction rate of this new ethanol synthesis reaction (ACS Applied Materials & Interfaces, Vol.7, 8398, 2015). With the characterization results on the prepared catalysts, rather higher ethanol synthesis rate can be expected. On the conversion of syngas to varied products, the capsule catalyst invented by us will be utilized to realize powerful one-step synthesis chemistry containing several catalytic reactions (Figure 2).

Development of Catalytic Transformation of Strong Sigma-Bonds

28

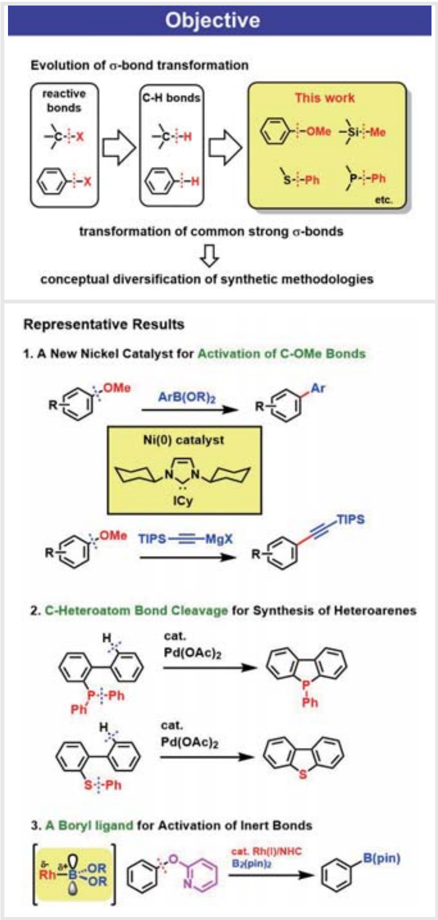
Principal Investigator (PI)

Mamoru TOBISU
Associate Professor, Graduate School of Engineering,
Osaka University

Synthetic chemists depend heavily on the transformation of reactive chemical bonds, such as carbon-halogen bonds and pai-bonds. This dependence significantly limits the diversity of synthetic methodologies that are available to synthetic chemists. To overcome this dependence, our research program focuses on the development of catalyst technologies that enable the transformation of strong chemical bonds and thus significantly diversify the synthetic methodologies.

1 Cross-coupling via C-O bond activation of anisoles

The catalytic transformation of anisole derivatives via the loss of a methoxy group has been developed. The key to success is the choice of the ligand. We have revealed that an N-heterocyclic carbene (NHC) ligand bearing relatively flexible cyclohexyl groups performs best in the cross-coupling of anisoles with a series of nucleophiles. This catalytic system is 10 times more reactive than the previously reported system using a phosphorus-based ligand. More importantly, this catalytic system allows for cross-couplings with nucleophiles that have never been possible before. For example, the first alkynylation and alkylation other than methylation or trimethylsilylation have been realized using our nickel catalyst in conjunction with a cyclohexyl-substituted NHC ligand. The developed catalytic system permits anisoles to be used, not only as economical and ecological alternatives to aryl halides, but also as versatile handles for late-stage functionalization reactions thanks to the robustness of a methoxy group under various synthetic conditions.



2 Heteroarene synthesis via carbon-heteroatom bond activation

The synthesis of heteroarenes, which constitute a previliged class of scaffolds with numerous applications, normally requires the use of highly reactive heteroatom-based reagents. We have developed new catalytic methods that do not require the use of such user-unfriendly reagents but, rather, involve the use of stable and readily available heteroatom-containing compounds such as tertiary phosphines or diaryl sulfides, allowing for rapid access to a range of elaborate heteroarenes. For example, it was found that a palladium(II)-catalyzed reaction of orho-biphenylphosphines, which are structurally simple tertiary phosphines bearing no reacive functional group, leads to the formation of dibenzophospholes. Notabley, this catalytic reaction proceeds through the cleavage of two kinds of inert chemical bonds, carbon-hydrogen and carbon-phosphrus bonds. It was also found that the corresponding biphenyl sulfides and selenides undergo cyclization through carbon-sulfur and carbon-selenium bonds to form dibenzothiophens and dibenzoselenophenes, respectively.

3 Inert bond activation using boryl-metal species

A boryl ligand has unique features including the presence of a vacant p-orbital and strong sigma-donation characteristics, which allow the unique metal/boron cooperative activation of inert molecules. For example, it was possible to realize the catalytic borylation of aryl aryl 2-pyridyl ethers using such a cooperative activation strategy. A rhodium-catalyzed reaction of aryl 2-pyridyl ethers with a diboron reagent leads to the formation of arylboronic esters. This reaction proceed through the cleavage of an aryl-oxygen bond, and a more reactive pyridyl-oxygen bond is not cleaved under these conditions. This unique regioselecivity is presumably the result of a unique rhodium/boron cooperative mode of activation. Since a 2-pyridyl group is used as a useful ortho directing group in carbon-hydrogen bond activation reactions, our borylation protocol allow a 2-pyridyl group to serve as a convertible directing group. We have also developed a new catalytic carbon-boron bond formation reactions using a diisopropylaminoborane reagent. The uniqueness of this reagent is that it contains two boron-hydrogen bonds to be used for new bond formations.

Creation of Methanol Synthesis Catalysts Working at Room Temperature Based on Mechanistic Principles of CO_2 Activation

29

Principal Investigator (PI)

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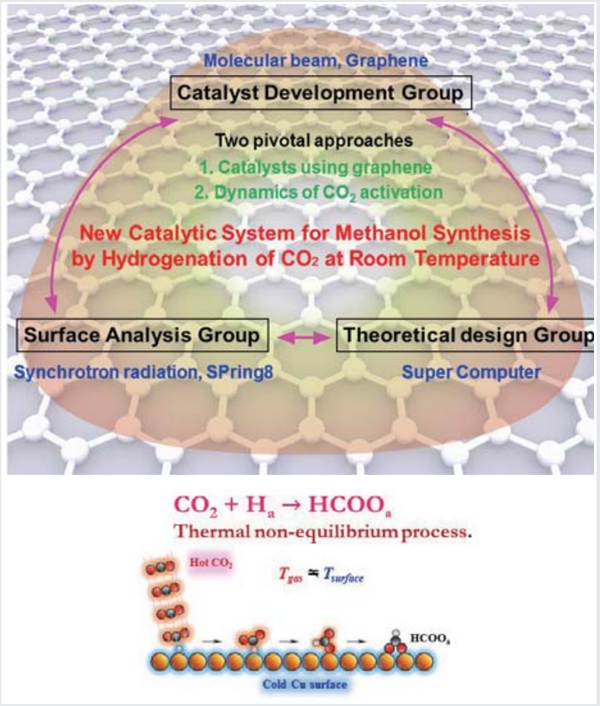
The purpose of the project is to establish an innovative catalytic system to produce methanol at room temperature by hydrogenation of CO_2. That is, based on surface reaction dynamics, surface reaction mechanism, and surface electronic states, we propose new ideas to synthesize methanol at room temperature. To this end, we study the detailed surface catalytic functions by examining surface reactivity at atomic levels using supersonic molecular beam machines, cutting-edge surface analytical apparatuses in synchrotron facilities, and super computers.



1 Thermal non-equilibrium dynamics of CO_2 hydrogenation

It has been clarified that formate synthesis by reaction of gaseous CO_2 with surface hydrogen atom on Cu surfaces, which is the initial elementary step of methanol synthesis, is a thermal non-equilibrium process by supersonic molecular beam experiments and density functional theory (DFT) calculations. That is, supplying translational and vibrational energies to gaseous CO_2 leads to production of formate on Cu at the surface temperatures below 200K without heating Cu catalysts. We thus overcome the first target to realize the room temperature synthesis of methanol. The second target is to let hydrogenation of formate to methanol proceed at room temperature. We currently pursue the room temperature hydrogenation of formate based on surface science experiments as well as DFT calculations. Meanwhile, we have developed a novel reactor as an application of the thermal non-equilibrium dynamics, by which we try to produce methanol by illuminating supersonic H_2/CO_2 onto catalysts kept at room temperature. We have just finished manufacturing the machine and started reaction tests.

2 Analysis of surface elementary steps of methanol synthesis

The elementary steps of methanol synthesis have been studied by photo emission spectroscopies using synchrotron facilities and DFT calculations. More specifically, dissociation of CO_2, decomposition of formic acid, and hydrogenation of CO_2 have been studied on a clean and Zn-deposited Cu surfaces in terms of the kinetics and the potential diagram. It was clearly observed in the experiments that CO_2 dissociates on the step and kink sites of Cu surfaces below 200 K. DFT calculations suggest that presence of water catalyze the dissociation of CO_2. It is expected that the findings lead to a low temperature activation system of CO_2.

3 Low-temperature methanol-synthesis catalysts using graphene

We apply graphene as a 2-dimensional conductive sheet to catalyst supports. Graphene has revealed very unique characters as a new type of catalyst support. That is, significant modification in catalytic properties of metal nanoclusters is observed due to the support effect of graphene. On the other hand, Pd nanoclusters were found to be formed spontaneously on graphene at a high loading as 70 wt% by just mixing graphene and Pd precursors such as $PdCl_2$ in water. The mechanism has been found to be an electrochemical reaction that reduction of Pd ions and oxidation of graphene by water take place simultaneously on a graphene sheet. This suggests that the conductive graphene sheet can be applied to electrochemical reactions as a 2-dimensional conductive catalyst support.

Creation of Artificial Photosynthetic Systems by the Fusion between Molecular Catalysts and Surface Science

30

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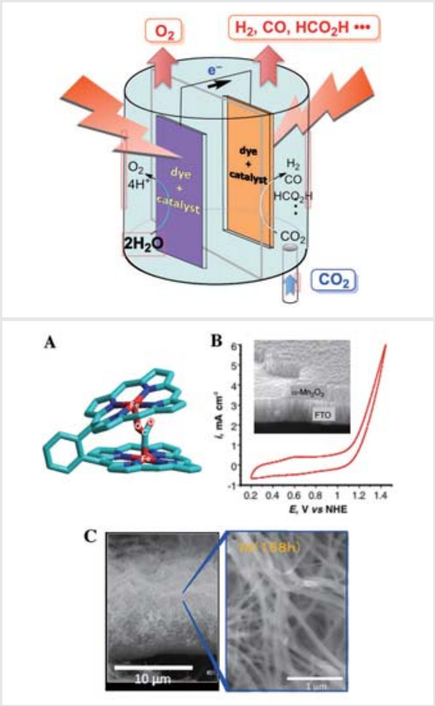
This project primarily aims to produce solar hydrogen as well as useful carbon resources from water and carbon dioxide, respectively, by a chemical conversion of solar energy. To realize these goals, firstly, catalysts, being capable to show high catalytic activity, low overpotentials, and high catalytic turnover frequencies and robustness, are developed. Dye-sensitized systems coupled with water oxidation and/or carbon dioxide reduction catalysts is one of the potential ways to convert photon-energy to chemical ones both at the anode and at the cathode. For these purposes, titanium oxide electrodes with nano-structured surface are developed.



1 Successful preparation of new CO_2 reduction catalysts

In carbon dioxide reduction, it is deserved that the catalysts have low overpotentials, high catalytic turnover frequencies, high product selectivity, without use of precious metals. Referring the structure of a metalloenzyme, carbon monoxide dehydrogenase (CODH), which can convert CO_2 in a very low overpotential to CO, we developed new catalysis that enable the selective conversion of CO_2-to-CO at low overpotentials and high catalytic turnover frequencies as well as excellent robustness with use of iron porphyrin dimers keeping the two Fe ions in suitable separation distances. This newly developed dinuclear iron catalysts are superior than the reported mononuclear ones in every aspects. This dinuclear motif as CO_2 reduction catalysts shows the new criterion for CO_2 reduction catalyst design. These iron catalysts can be fixed on an electrode through chemical bonds and can be applied for artificial photosynthesis.

2 Preparation of thin-film manganese oxide electrodes for water oxidation and the elucidation of their reaction mechanism

Manganese oxides are interested from the similarity with oxygen-evolving $CaMn_4O_5$ core in plant photosynthetic system II. Among various manganese oxides, α-Mn_2O_3 can catalytically oxidize water to O_2 at a relatively low overpotential and is superior than MnO_2. It, however, has been known only the preparation of its power form. We developed a new method to modify it as a thin-film on any electrodes in an arbitrary thickness and optimized its performance and robustness as a water-oxidation electrode. The resultant electrode can be used for water oxidation at a neutral aqueous solution at overpotential $\eta > 0.2$ V and attained current density > 1 mA/cm^2 for more than 12 h without any current drop and the film detachment. This thin-filmed catalyst also enables the spectroscopic assignment of its high-valent states such as $Mn^{IV}{=}O$ and $Mn^{V}{=}O$. With use of this advantage, we elucidated the active intermediate, which oxidizes water, to be $Mn^{V}{=}O$ by spectroscopic and kinetic methods. This is the first example for the assignment of the active Mn species in catalytic water oxidation with inorganic manganese oxide catalysts.

3 Development of titanium metal modification having gradient and nano-structured surface for electrodes

Sintered layers of titanium oxide nano particles are used for the charge accepting material as a bottom-up method in dye-sensitized solar cells. In this titanium oxide layer, its electron diffusion coefficient is generally limited at most 10 μm. Our team has developed the preparation of nano-structured surface modification method of titanium metal as a top-down method. The resultant micro-fibers are grown on the titanium base and its nano-structured layer can be tunable. These materials realized the following characters, which are essential for the dye modification on them; (1) successful preparation of a nano-structured layer more than 10 μm thickness has a large surface area, (2) by the optimization of heating and environmental conditions, this layer shows good electron conductivity as well as capability of chemical modification of various materials on tits surface by keeping its surface composition to be anatase titanium oxide. These characters are adequate for dye modification and are expected to be applied it for photosensitized charge separation materials.

Invention of The Phenacene-Type π-Electronic Organic Molecules for Electronic Energy Devices Based on the Creation of Catalysts

31

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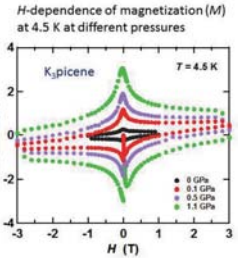
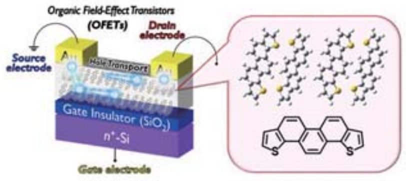
In this research project, we focus on the synthesis of "new types of phenacene molecules with the extended π-electronic systems", in particular, polycyclic hydrocarbons directed toward an efficient electronic energy devices such as superconductive materials, field effect transistors (OFET), and organic photovoltaics (OPV). The physical properties of the organic compounds synthesized by the innovative activation and formation of the chemical bonds using transition-metal catalysts are thus evaluated.





1 Synthesis of Phenacene Derivatives

The transition-metal-catalyzed cross-couplings and cyclization reactions were utilized to synthesize picene, a compound consisting of five fused benzene ring with an armchair structure and its derivatives. Ruthenium-catalyzed direct arylation of C-H bonds followed by the bismuth-catalyzed arylative cyclization were utilized to synthesize picene ([5]phenacene), a compound consisting of five fused benzene rings with an armchair structure and its derivatives. Using the similar transformation, the number of fused-benzene ring can be easily increased up to seven to afford [6]- and [7]phenacenes. A facile synthesis of ethene-bridged terthiophenes (EBTTs) using a double Sonogashira coupling and a following cyclization reaction was also accomplished. We further designed terthiophenes bearing two or four bromide as key precursors, and developed regioselective Negishi cross-coupling reactions and the sequential Buchwald-Hartwig coupling reactions leading to the compound which have three thiophene rings fused with two pyrrole rings. In addition, we replaced the two terminal benzene rings with thiophene rings to yield phenanthro[1,2-*b*:8,7-*b'*]dithiophene (PDT). The reaction could be readily carried out in gram scale. These analogous molecules of picene are expected to show the better physical properties than picene.

2 Development of Superconducting Materials

During this project, we also aim at making not only new superconductors with the T_c being as high as possible but the superconductors with the high superconducting volume-fraction. This would open an avenue for new superconductor science. Recently, we found new superconducting phases in $K_x$picene and rubidium-doped picene (Rb_xpicene), whose T_c's were 14 and 11 K, respectively. The features of new phases are currently investigated in this project. The T_c of 14 K phase of $K_x$picene increased with increasing pressure, and the T_c reached 19 K at 1.1 GPa, The shielding fraction also increased with applying pressure, and it reached 18.5% at 1 GPa. The superconducting phase was characterized by energy dispersive X-ray spectroscopy (EDX), X-ray diffraction pattern and time-of-flight mass spectroscopy, indicating a K doped picene. Furthermore, the superconductivity in graphene and graphite has been pursued in this project. The Ca / K intercalated graphite, $Ca_xK_{1-x}C_y$ showed the superconductivity, which exhibited KC_8-type structure at $x \neq 1$. This means that the KC_8 structure can also provide the T_c higher than 5 K.

3 Application to Transistors and Photovoltaics

A wide variety of substituents could be introduced on the phenacene core, and the physical characters of these compounds could be controlled by the substituents. For instance, when we fabricated the thin-film FET devices of some alkylated PDTs by a vapor deposition, the p-channel FET characteristic was shown with the values of hole mobility up to 2.19 $cm_2 V^{-1} s^{-1}$. The final goal of the work is to realize the multifunctional/high-performance transistor chip using aromatic hydrocarbon or graphene for future ubiquitous electronics.

Moreover, the low-band gap semiconducting polymers containing a PDT core in the polymer backbone have been synthesized. These PDT-based polymers have some superior features, including strong intermolecular interaction, high thermal stability, deep HOMO energy levels, and dense packing structure in the solid state. The solar cell devices using PDT-isoindigo (IID) copolymer or PDT-benzothiadiazole (BT) exhibited high power conversion efficiency (PCE) with 5.28% and 6.56%, respectively. In particular, PDT-BT copolymers formed a desirable face-on orientation, which can promote the efficient carrier transport in solar cells, reading to high PCE.

Precise Synthesis of New π Conjugated Star Molecules by Highly Efficient Catalytic Carbon-Carbon Bond Formation, and their Application as Optical Materials Based on Integration of Functionality

32

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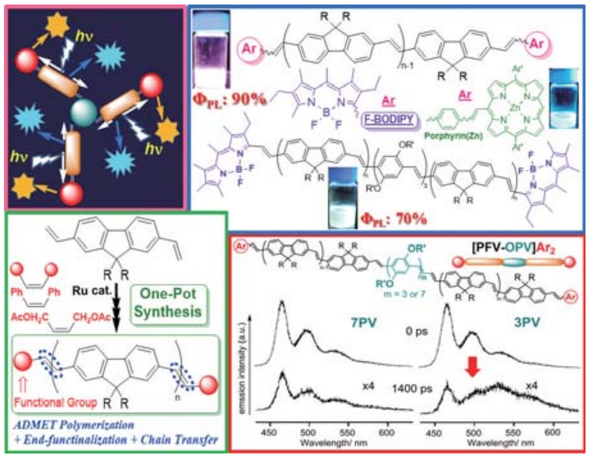

Purpose on the present project is synthesis of end-functionalized π-conjugated organic molecules (polymers, oligomers) by highly efficient catalytic carbon-carbon bond formation and their application as unique optical materials. The present project also aims for precise synthesis of new star, ball shape fully π-conjugated organic molecules and their application as the unique functional materials on the basis of precise integration of functionality. Development of the efficient synthetic methods/strategy has been considered to play a key role for success of this purpose.

1 Precise synthesis of end functionalized polymers

Acyclic diene metathesis (ADMET) polymerization afforded defect-free, all-*trans* polymers, poly(arylene vinylene)s, and the resultant polymers prepared by ruthenium-carbene catalysts possessed vinyl groups at the chain ends. Various end functionalities can be thus introduced exclusively by treatment of the vinyl group with olefin metathesis using molybdenum catalysts followed by Wittig-type coupling with aldehyde. Poly(9,9-dialkyl-fluorene-2,7-vinylene)s (PFVs) containing chromophores (exhibiting white-light emission with high quantum efficiency) has been prepared. The emission properties can be modified not only by the PFV (conjugation) chain length, but also by nature of chromophore (end group) and the middle segment.

2 Precise one-pot synthesis of end-functionalized block copolymers, star-shaped polymers

Synthesis of a series of fully conjugated end-functionalized block and star-shape (triarm) polymers, and the triblock copolymers have been successfully demonstrated on the basis of quantitative carbon-carbon bond formation (olefin metathesis with the vinyl group and subsequent Wittig-type coupling). For example, a precise, one-pot synthesis of end-functionalized block copolymers consisting of PFVs and oligo(2,5-dialkoxy-1,4-phenylene vinylene) or terthiophene units as the middle segment have been prepared and identified. Effect of PFV conjugation length, middle segment and the end groups toward the emission properties have been studied. Time-resolved fluorescence study reveals that a dynamical structural relaxation in the excited state is proposed as the origin of time-dependence of the fluorescence spectra in the block polymer.

3 Precise synthesis of end-functionalized conjugated oligomers

Precise synthesis of *chemically, analytically pure* oligo(2,5-dialkoxy-1,4-phenylene vinylene)s (OPVs) with well-defined end groups, has been achieved. Their photoluminescence quantum yields are affected by the end groups rather than the number of repeating units. The OPVs containing chiral end groups exhibited unique aggregation induced circular dichroism (AICD) behaviors. OPVs containing different chiral alkoxy substituents on the end groups with structurally regular (all *trans*), controlled repeat units have been prepared; these showed highly enhanced aggregation-induced circular dichroism (formation of supramolecular polymers), and an inversion of CD signal was observed even with the same end groups under certain conditions.

4 Catalytic one-pot synthesis of end-functionalized polymers

Facile, one pot synthesis of end-functionalized conjugated polymers (EF-CPs) has been established by ADMET polymerization followed by chain transfer with internal bi-functional olefins in the presence of ruthenium-carbene catalyst. Another one-pot synthesis method using molybdenum catalysts has also been established recently.

Efficient Synthetic Access to Novel Pi-Conjugated Molecules and Development of their Function

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Principal Investigator (PI)

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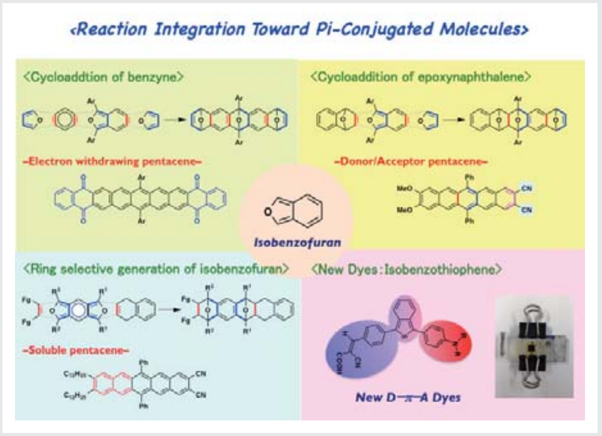
The purpose of this research is development of an efficient synthetic route to various pi-conjugated systems based on the reaction integration using the reactive molecules, having potentially attractive reactivities. Three kinds of activations by heat, light, and transition metal catalyst enable the selective construction of complex structures by introducing diverse functionalities.



1 Efficient synthetic access to isobenzofurans

Isobenzofuran is 10π electron system with a quinoid structure, which makes them useful intermediate for natural/unnatural product syntheses. In this context, an efficient one-pot synthetic method of diarylisobenzofurans has been developed via sequential nucleophilic addition of aryl Grignard reagents to 2-formylbenzoate. Moreover, 1,3-bis(arylethynyl)-isobenzofurans, a new π–extended molecule, was prepared by nucleophilic addition of alkynyllithium to benzocyclobutenone and subsequent oxidative ring cleavage of the four-membered ring. These products, thus obtained, would serve as useful building blocks for preparation of novel π-conjugated molecules.

2 Highly condensed aromatic compounds

Efficient synthetic routes to highly condensed aromatic compounds were developed by [4+2] cycloadditions of isobenzofuran with epoxynaphthalene and/or arynes. As a potentially versatile method for the rapid, selective assembly of functionalized polycycles, we also exploited the synthetic equivalent of bis-isobenzofuran, which enabled the iterative generation of isobenzofuran and subsequent functionalization and/or introduction of the fused ring by trapping with dienophile. Importantly, these reactions can be performed in a one-pot manner, efficiently affording various functionalized polycyclic aromatic compounds. Moreover, these methods would allow us to prepare various substituted pentacenes, including donor–acceptor type molecules with unique photophysical properties.

3 New D–π–A dyes

Based on the new synthetic method of isobenzofurans, an efficient synthetic route to isobenzothiophenes and isobenzoselenophenes was developed. Moreover, new D–π–A dyes with a unique quinoid structure were synthesized by using isobenzothiophene and isobenzoselenophene as a π–spacer, which showed typical photophysical properties and a good photovoltaic performances.

Development of the Synthetic Strategy for Bowl-Shaped π-Conjugated Molecules Utilizing Transition Metal-Catalyzed Reactions

34

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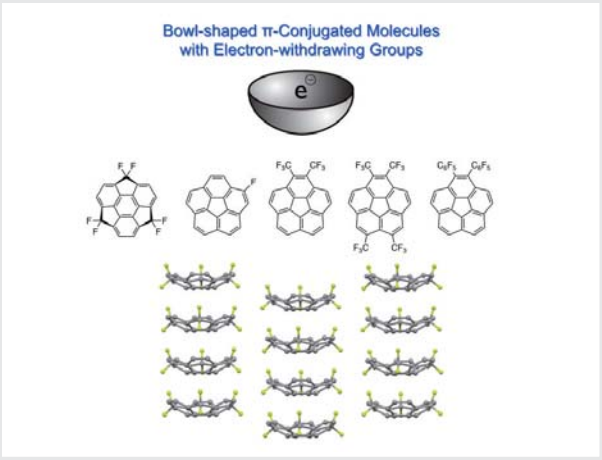
Bowl-shaped π-conjugated compounds, buckybowls, possess unique properties due to the special bowl shape, which are distinct from those of planar π-conjugated compounds. The buckybowls are expected to be potential organic materials by utilizing the unique properties. To extend the research on the properties and materials, it is required to develop the efficient method to synthesize the buckybowls possessing heteroatoms and functional groups. This project studies the efficient synthetic strategy for buckybowls by using transition metal-catalyzed reactions and the properties of these buckybowls.



1 Development of Bowl-shaped Molecules with high electron conductivity

Organic semiconductor is one of important materials in organic electronics and the development of excellent organic molecules with high conductivity has been extensively studied. Bowl-shaped molecules are also attractive molecules owing to the property as n-type semiconductor. To improve the conductivity, it is necessary to improve the electron-accepting ability. We synthesized bowl-shaped molecules with fluorine or trifluoromethyl substituents, since fluorine is known to possess strong electronegativity. The electron-accepting ability of these molecules was improved and they were found to exhibit high conductivity.

2 Development of Bowl-, Helix-, Butterfly-shaped Molecules with Excellent Redox Property

It is important to develop organic molecules with excellent redox property in organic electronics and the development of such organic molecules has been actively studied. We succeeded to develop bowl-, helix-, and buttery-shaped organic molecules with excellent redox properties. These molecules exhibited redox reaction in wide rage of potentials and repeated without degradation. In addition, helix-shaped molecules were found to undergo reversible disproportionation reaction with electron transfer by responding to external acid/base stimuli. It is of great interest to apply such external stimulus-responsive molecule to new organic materials.

3 Development of Bowl-shaped Molecule to Transform the Molecular Shape by Redox

Molecular machines are molecules or molecular composite to show controlled machinery movement by responding to external stimuli. Creation of artificial molecular machine is of great interest and has been extensively studied. We succeeded to develop bow-shaped molecule that transforms the molecular shape by electron-transfer redox reaction. This molecule with embedded nitrogen atoms possesses bowl structure in neutral state and changes to planar shape by removing electrons. In turn, it goes back to bowl shape by giving electrons. Since this molecule does not decompose during the change of shape and transfer of electrons, it can repeat the transformation. Application to molecular machine responding to external electric stimulus is expected.

Development of Highly Efficient Catalysts for Hydrogenation of Carbon Dioxide Based on Proton-Responsive Catalysts and Applications to Artificial Photosynthesis

35

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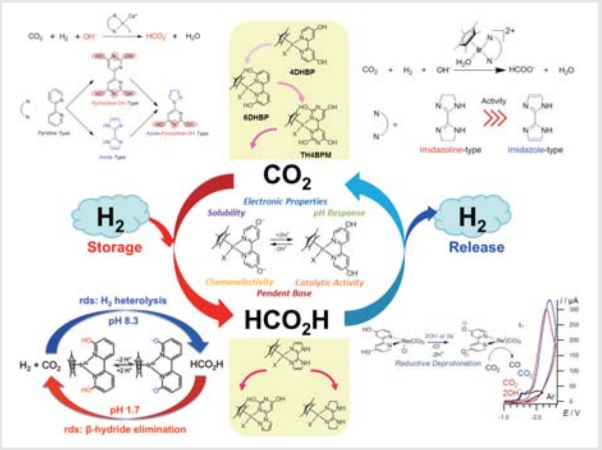

The purpose of this study is to develop highly efficient catalysts for CO_2 reduction for the production of liquid fuels and chemical feedstocks based on proton-responsive catalysts. Following the catalyst design concept of proton-responsive catalysts, our goal is the development of catalysts for CO_2 hydrogenation and dehydrogenation of formic acid that can work under mild reaction conditions such as room temperature and atmospheric pressure in water without organic additives.

1 Development of highly efficient catalysts with azole- and azoline-type ligands

Previously, we have developed catalysts having 4,4'-dihydroxyl-2,2'-bipyridine as a proton-responsive ligand, which are reversibly deprotonated to generate an oxyanion (–O–). The acid-base equilibrium of the phenolic hydroxyl groups in the pyridine ring imparts some unique properties to the complexes coordinated with these ligands. In particular, it was found that the electronic effect of an oxyanion enhances catalytic activity remarkably.

In past years, in order to improve the catalytic activities for CO_2 hydrogenation and dehydrogenation of formic acid, we have investigated the catalysts having an N-containing five-membered ring as a ligand instead of a pyridine moiety. As a result, the series of catalysts outperformed the bipyridine series in the both catalyses. Furthermore, introduction of hydroxyl group into the ligands led to the enhancement of catalytic activity. Interestingly, an imidazoline moiety as a ligand was effective for both catalysis. The catalyst having bisimidazoline exhibited the turnover frequency of 43 h^{-1} in hydrogenation of CO_2 under atmospheric pressure and room temperature. The catalytic activity was comparable to that of the most effective dinuclear complex (70 h^{-1}) that we developed. These results will contribute to the development of novel catalyst designs for CO_2 hydrogenation.

2 Mechanistic insight of hydrogenation of CO_2 and dehydrogenation of formic acid by DFT calculation

Recently, Cp*Ir complexes with proton-responsive bipyridine ligands capable of reversible hydrogen storage via interconversion between H_2/CO_2 and formic acid/formate in water have been reported. This interconversion is performed via CO_2 hydrogenation and FA dehydrogenation reactions and modulated by the pH of the medium. We performed a computational investigation of the mechanistic aspects of reversible hydrogen storage via two of these catalysts: namely, $[Cp^*Ir(4DHBP)]^{2+}$ (4DHBP = 4,4'-dihydroxy-2,2'-bipyridine) and $[Cp^*Ir(6DHBP)]^{2+}$ (6DHBP = 6,6'-dihydroxy-2,2'-bipyridine). Distinct features of the catalytic cycles of $[Cp^*Ir(4DHBP)]^{2+}$ and $[Cp^*Ir(6DHBP)]^{2+}$ for CO_2 hydrogenation and FA dehydrogenation reactions were demonstrated using density functional theory (DFT) calculations employing a "speciation" approach and probing deuterium kinetic isotope effects (KIE). Finally, we have examined the different aspects of computational methods employed for mechanistic investigation of CO_2 hydrogenation and formic acid dehydrogenation reactions and have provided recommendations regarding the level of a theory to be employed and the geometry optimization protocols. In addition to the mechanistic insights and principles for the design of improved next-generation catalysts, the validation of computational methods for the investigation of the hydrogenation and dehydrogenation reactions is addressed.

Novel Activation and Synthetic Transformations of Stable Chemical Bonds by Means of Metal Catalysts

36

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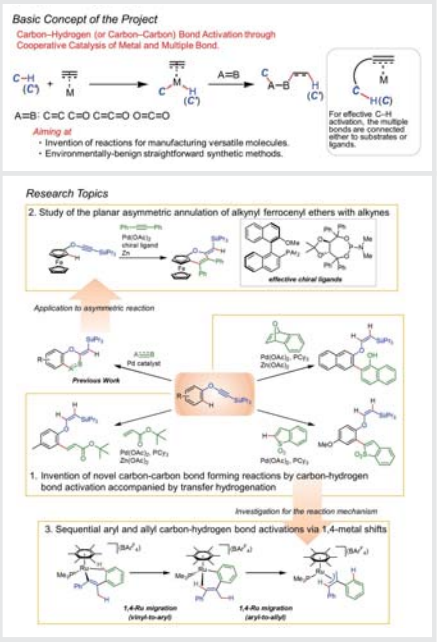
Organic synthesis based on the step economical and highly selective transformation is essential for invention of novel organic materials and for realization of sustainable society based on green chemistry. In view of this, selective carbon–hydrogen bond functionalizations in organic molecules are becoming more important. The present project aims at invention of methods for the activation of stable chemical bonds such as carbon–hydrogen bonds by the combination of transition metal catalysts with a multiple bond to achieve new carbon–carbon bond forming reactions. The novel methodology allows us to construct useful target molecules such as π-electron conjugated systems.

1 Invention of novel carbon-carbon bond forming reactions by carbon-hydrogen bond activation accompanied by transfer hydrogenation

Cross-dehydrogenative bond-forming reactions are highly attractive methods in the toolbox of synthetic organic chemistry, showing a great promise in terms of atom and step economy. We have demonstrated that an alkynoxy group ($-OC\equiv CR$) is utilized as a directing group for adjacent C–H bond activation and as an acceptor for C–H bonds. In this study, we have found alkynoxy-mediated cross-dehydrogenative carbon-carbon bond formation reactions take place via the cleavage of two C–H bonds followed by the transfer hydrogenation of the alkynoxy group. Alkynyl aryl ethers react with 1,4-epoxy-naphthalene to give a binaphthyl derivative having a (Z)-TIPS-ethenyloxy group. In cases of *tert*-butyl acrylate instead of 1,4-epoxy-naphthalene, the corresponding *ortho*-alkenylated product was obtained. Moreover, we aim at the invention of dehydrogenative cross-coupling reaction. We have found that the reaction of alkynyl aryl ethers with benzothiophene oxide takes place site-selective cross-coupling via double C–H bond cleavage in both substrates to give an *ortho*-heteroarylated product. The present reaction system is characterized by a site selective C–H bond cleavage and dispenses the use of an additional oxidant or base to trap the hydrogen atoms.



2 Study of the planar asymmetric annulation of alkynyl ferrocenyl ethers with alkynes

We have applied the annulation reactions using alkynyl aryl ethers developed by Hiyama group to asymmetric synthesis. Since last year, we focused our attention on ferrocene compounds which are utilized as catalysts, ligands, and functional materials due to their electronic and structural properties. Last year, Fukuzawa group has already developed the reaction of alkynyl ferrocenyl ethers with inner alkynes through C–H bond activation to give ferrocenopyran derivatives. In this study we mainly examined the planar asymmetric reaction of alkynyl ferrocenyl ethers with diarylalkynes catalyzed by a palladium catalyst. After screening of a variety of chiral ligands including a series of ClickFerrophos ligands uniquely-developed by us, it has been revealed that MOP as a binaphthyl type ligand and phosphoramidites derived from tartaric acid are suitable for the planar asymmetric reaction of TIPS-ethynyl ferrocenyl ether with diphenylacetylene to give the corresponding chromano[*e*] ferrocene with moderate planar enantioselectivity.

3 Sequential aryl and allyl carbon-hydrogen bond activations via 1,4-shifts

We assume that novel reactions can be invented by understanding the detailed reaction mechanisms for the annulations using alkynyl aryl ethers and above-described alkenylation and arylation via the transfer hydrogenation. Especially, understanding of the reactivity of alkenylmetal complexes should be needed. Ishii group revealed a continuous aryl and allyl C–H bond activations by a sequential 1,4-metal shifts from a *cis*-2-phenyl-1-propenylruthenium complex. That is, the ruthenium center in this complex takes part in the vinyl-to-aryl 1,4-migration and the resultant *o*-vinylaryl complex isomerizes slowly at room temperature to afford the corresponding η^3-allyl complex through the rotation of the C_{aryl}–C_{vinyl} bond and the second aryl-to-allyl 1,4-Ru migration. These reactions provide the first example of the 1,4-metal migration of a group 8 metal center. The η^6-C_6Me_6 ligand is considered to play a key role in the present reaction, and switching the η^6-arene ligand to differently substituted arenes is expected to lead to different transformation. Further investigation towards the catalytic version of the present transformation is now in progress.

Chemo-, Regio-, and Stereoselective Carbon–Carbon Bond Forming Processes using Innovative Alkene Oxidative Coupling Strategies

37

Principal Investigator (PI)

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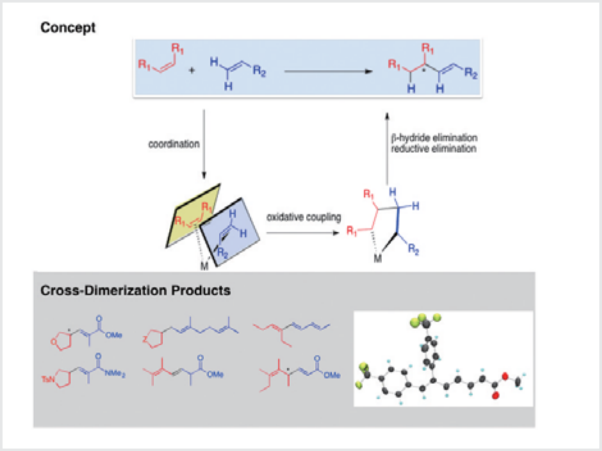
In this project, we develop linear cross-dimerizations using substituted alkenes with high chemo-, regio-, and enantioselectivities. This is a selective carbon-carbon bond forming reaction with perfect atom and step economy. The key mechanism for the present project is the oxidative coupling mechanism at a Ru(0) center to from a ruthenacycle using substituted alkenes/alkynes and/or conjugated compounds. Because the β–hydride elimination from the resulting ruthenacycle is a quick reaction, the subsequent reductive elimination provides a linear coupling product. We will develop the new horizon of the coupling reactions using substituted alkenes and conjugated compounds.



1 C3-Selective Substitution Reactions of Unsaturated Heterocyclic 5-Membered Ring Compounds

C2-Selective introduction of substituents to a 5-membered heterocyclic ring compound has been widely studied. However, such a direct substitution reaction at the C3-position remains unexplored. In this project, we have developed C3-selective coupling reactions of 2,5-dihydrofuran and 2,5-dihydropyrrole derivatives with conjugated carbonyl compounds and conjugated dienes under mild conditions. In this reaction, a conjugated compound and a substituted alkene selectively coordinate to a formal 12e Ru(0) species to satisfy the 18e rule. This is the key for the cross-dimerization in this reaction. The carbon-carbon bond forming reaction proceeds by the oxidative coupling mechanism. There are many biologically active species for the C3-substituted heterocyclic 5-membered ring compounds and the present reactions provide a new and straightforward synthetic route to give many biologically active lead molecules.

2 Enantioselective Cross-Dimerizations using Substituted Alkenes

Enantioselective carbon-carbon bond formation reactions are one of the ultimate goals in synthetic organic chemistry. However, most of the pioneering works have problems for the atom and step economy, and the enantioselective formation of acyclic compounds is still rare. Moreover, formation of a center-chiral compound from substituted alkenes is unprecedented. If two different substituted alkenes are selected chemoselectively, and coordinate to the metal center with a high prochiral selectivity, under the control of their rotamers, the subsequent oxidative coupling reaction and β–hydride elimination/reductive elimination would provide a chiral compound. In this project we have developed novel enantioselective carbon-carbon bond formation reactions by the oxidative coupling mechanism. In fact, the coupling reaction of 2,5-dihydrofuran with methyl methacrylate catalyzed by a chiral Ru(0) complex gave the cross-dimer in 74% yield with 80% ee.

3 Straightforward Synthesis of Conjugated Trienes.

The coupling reactions of conjugated dienes with alkynes are known to produce enynes. The coupling reactions between an alkyne and two equiv of methyl acrylate, or between two equiv of internal alkyne and a methyl acrylate are known to give the conjugated triene compounds. However, the scope of these pioneering examples is limited because methyl acrylate is indispensable for these reactions. In this project, we found that the linear corss-dimerization between conjugated dienes with substituted alkynes gave conjugated trienes with perfect atom and step economy. In this reaction, a substituted alkyne formally inserts into the C-H bond in the terminal methylene position in conjugated diene. This reaction is a *syn*-selective hydrocarbonation of alkynes. Although only internal alkynes are available in this reaction, this reaction has a wide scope of alkynes and conjugated dienes with regard to the electron-rich and –deficient nature of these substrates. For example, reaction of diphenylacetylene with methyl pentadienoate was catalyzed by Ru(naphthalene)(1,5-COD) (10 mol%) to give (2*E*,4*E*,6*Z*)-methyl 6,7-diphenylhepta-2,4,6-trienoate in 84% yield at room temperature within 10 min.

Development of Advanced Molecular Transformation Technology Based on Design of Environmental Benign Redox Systems Consisting of Early Transition Metals

38

Principal Investigator (PI)

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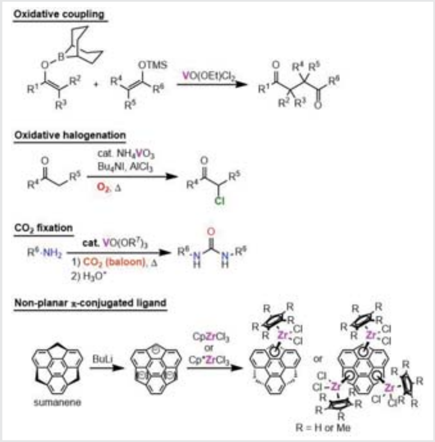
Construction of the catalytic systems based on redox-active and/or Lewis acidic properties of early transition metals is investigated in this project. A purpose of the investigation is the creation of advanced molecular transformation technology through the control of electron transfer processes and nano-space for reactions. Through the study, development of the environmental benign catalytic systems is directed from the viewpoint of utilization of molecular oxygen as a terminal oxidant and carbon dioxide as a C1 unit.



1 Development of selective oxidative cross-coupling of enolates

Oxovanadium(V)-induced selective oxidative cross-coupling of enolate compounds was developed. This method is clearly beneficial because valuable unsymmetric 1,4-dicarbonyl compounds can be directly synthesized from the corresponding ketones. One of the keys for this reaction system is the choice of the combination of boron and silyl groups as metals for the enolates to discriminate their reactivities. The protocol for reductive cross-coupling was also achieved.

2 Development of oxidative halogenation

Halogenation reaction is one of the most important reactions in the field of organic synthesis, providing versatile precursors and substrates in a variety of coupling reactions. The catalytic halogenation reaction without the use of explosive and toxic strong oxidants was achieved by using a commercially available inexpensive ligand-free vanadium catalyst with molecular oxygen as a terminal oxidant. A catalytic chlorination of ketones was performed by using a vanadium catalyst in the presence of Bu_4NI and $AlCl_3$ under atmospheric molecular oxygen. This catalytic chlorination could be applied to the chlorination of ketones and alkenes. In the case of the chlorination of alkenes, the corresponding vic-dichlorides were obtained in good yields. $AlCl_3$ was found to serve as both a Lewis acid and a chloride source to induce the facile chlorination. The combination of Bu_4NI and AlI_3 in the presence of a vanadium catalyst under atmospheric molecular oxygen was found to induce the iodination of ketones.

3 Development of catalytic transformation system by using carbon dioxide as C1 unit

Urea derivatives are useful compounds for herbicide, pesticide and raw materials of resin. In general, urea derivatives are prepared by the reaction of the corresponding amine with toxic phosgene or carbon monoxide. We have already demonstrated the one-step synthesis of imidovanadium(V) compounds by the reaction of amines with oxovanadium(V) compounds. The reaction of imidovanadium(V) compounds with carbon dioxide is expected to give the corresponding urea derivative. Commercially available inexpensive ligand-free oxovanadium(V) catalyst was demonstrated to catalyze the atmospheric CO_2 fixation reaction in the presence of amine to give the corresponding urea derivative. Catalytic formation of a variety of urea derivatives was performed by using oxovanadium(V) catalyst and carbon dioxide as a C1 building reagent in the presence of i-Pr_2EtN as a base and molecular sieve (MS 3A) as a dehydrating agent. The preparation of urea derivatives using carbon dioxide as a carbonyl source has attracted much attention because of nontoxic, abundant, and economical characteristics.

4 Design and application of the non-planar π-conjugated molecule ligand for early transition metal

Sumanene is a C_3-symmetric fullerene fragment molecule with a non-planar π-conjugation. This molecule is characterized by the three benzylic positions, where anion can be stabilized. Furthermore, the generated anions behave as a cyclopentadienyl-like anion. Therefore, sumanene can be used for a non-planar cyclopentadienyl-like ligand. The mono- or tricyclopentadienyl-like anion was trapped with cyclopentadienyl zirconium trichloride, resulting in the corresponding mono- or trizirconocene dichloride complex. The complexation took place from the convex face of the bowl structure. Such zirconocene complexes may be of potential catalytic utility as a novel type of catalyst.

The carbonization of π-conjugated compounds such as polyaniline is also studied toward the development of catalyts for oxygen reduction reaction on the cathode of fuel cell.

Development of Functional Nonplanar π-Electron Systems Utilizing Butadiene as a Key Building Unit

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Principal Investigator (PI)

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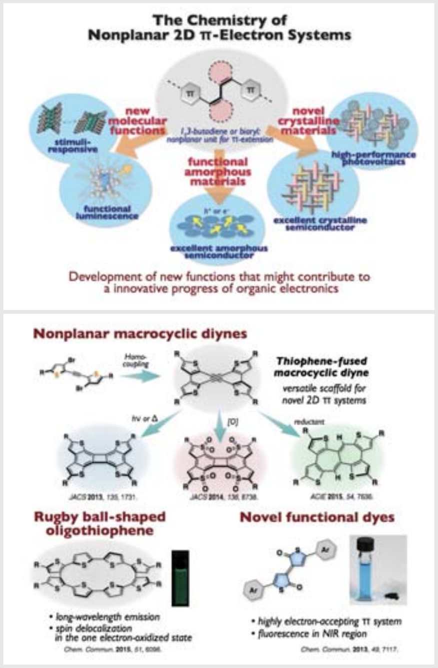

Development of a novel π-conjugated skeleton with a characteristic electronic structure as well as optimal intermolecular interactions in the condensed phase is of importance for the superior optoelectronic properties such as intense luminescence and high charge-carrier mobility. However, there is a wide gap between the development of novel π-conjugated skeleton and the practical application for organic electronics probably due to the difficulty in the prediction of the solid-state properties. Aiming at the control of the molecular alignment and thus physical properties of π-electron systems in the solid state, this research project proposes a molecular design based on the nonplanar molecular structure. Basic idea is to create novel nonplanar π-electron systems by bridging two or more π-conjugated chains with nonplanar π units such as butadienes and biaryls, which exhibit nonplanar structures with extended π conjugation. By taking advantage of these molecular structures, we will tackle the control of the molecular alignments and thus the intermolecular interactions, giving rise to excellent optoelectronic properties in the solid state.

1 Efficient synthesis of nonplanar macrocyclic diynes and their unusual reactivity

In the past three years of this project, we tried the synthesis of a series of novel π-electron systems linked with the 3,3′-bithiophenes as a nonplanar π unit. First, we have succeeded the efficient large-scale synthesis of the nonplanar macrocyclic diyne linked with the 3,3′-bithiophene units (*JACS* **2013**). This nonplanar macrocyclic diyne exhibits characteristic photophysical properties due to the effective π conjugation through nonplanar π unit. Furthermore, it undergoes the transannular [2+2]-type cycloaddition by either photoirradiation or mild heating, leading to the formation of the seven-ring-fused 2D π electron system, which has a potential for the p-type semiconducting material. Importantly, we revealed that this reactivity is owing to not only the close proximity of two alkyne moieties but also the moderately low aromaticity of fused thiophene rings. Based on this finding, we also reported that the dearomatization of the fused thiophene rings by the oxidation of sulfur atoms significantly facilitate the cyclization under the thermal condition (*JACS* **2014**). Moreover, we demonstrated that the same macrocyclic dyne undergoes different mode of transannular cyclization upon the reduction with Na metal, producing thiophene-fused heptalene (*ACIE* **2015**). The produced novel 2D π systems exhibit significant potential as building blocks for the functional materials due to their multi-redox properties as well as unusual structural features.

2 The chemistry of rugby ball-shaped cyclic oligothiophene

Oligothiophenes represent a well-established scaffold for π-electron materials because of their great potential for a wide variety of applications in organic electronics. Most of the oligothiophenes reported to date contain thiophene units catenated in the α-positions mostly because the π-conjugation is effectively extended through these linkages. On the other hand, linkage in the β-positions affords oligothiophenes with higher structural versatility. From this viewpoint, we have recently designed and synthesized the rugby ball-shaped cyclic oligothiophene composed of two α-quarterthiophene units connected at β,β'-positions, and demonstrated its intriguing elliptical structure which is different from previously reported cyclic α-oligothiophenes. Reflecting reflecting its structural features, this cyclic oligothiophene exhibits a set of unusual photophysical and electrochemical properties, such as red-shifted fluorescence as well as multi-redox properties (*Chem. Commun.* **2015**).

3 Development of novel functional organic dyes utilizing 3,3'-bithiophene derivatives as a key precursors

Making use of the 3,3'-bithiophene-based π-conjugated compounds as key synthetic intermediates, we recently developed a new series of functional organic dyes composed of the cross-conjugated thiolactone moieties, "S-Pechmann dyes" (*Chem. Commun.* **2013**). S-Pechmann dyes exhibit not only the long-wavelength absorption and emission, but also the significant electron-accepting character comparable to fullerene C_{60}. We are now pursuing the possibility of S-Pechmann dyes as a key building block for functional materials.

Highly Efficient Hybrid Photocatalysis for Solar CO_2 Reduction

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Principal Investigator (PI)

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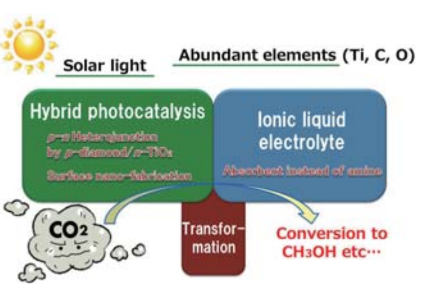
This project aims to develop solar photocatalytic processes for realizing highly efficient CO_2 conversion, in which catalytic materials consisted of abundant elements are environmentally-friendly applied. Photoelectrodes with pn heterojunction of high quality of polycrystalline $TiO_2$and diamond are developed following application of ionic liquids as electrolytes. Our goal is eventually to create the fundamental technology of novel solar CO_2 reduction processes.



1 Development of pn heterojunction photoelectrode

Photocatalysis opened a new era in the field of solar energy conversion and storage. We now developed the pn heterojunction photoelectrode using of p-type lightly boron-doped diamond and n-type TiO_2 for enhancing the photoelectrochemical activities. Semiconductive diamond film was at first deposited on silicon substrate by microwave plasma CVD method, and then thin film of TiO_2 was sputtered on the diamond surface by reactive sputtering method at mild conditions to keep the diamond properties. The microstructural analysis showed a uniform deposition of anatase structure of TiO_2 and its thickness can be controlled by varying the sputtering duration. The current to voltage measurement at ambient temperature revealed the formation of pn heterojunction. The rectifying property of 6.4×10^4 at ± 5 V was remarkably superior, and this small leakage current at high voltage was achieved on the uniform pn junction at TiO_2 thin film by sputter duration at 90 min. Photocatalytic performance of this suitably formed photoelectrode was photoelectrochemically evaluated by water splitting property, showing 1.6 fold higher activity compared with bare n-type TiO_2 photoelectrode. This enhanced photoelectrochemical performance at pn heterojunction electrode attributed in the injection of hole from p-type diamond to n-type TiO_2, which increases carrier separation and thereby enhances the photoelectrochemical performance.

2 Development of selective CO_2 reduction assisted by ionic liquid

Utilization of atmospheric CO_2 for energy conversion and storage is one the ways to maintain a balanced carbon cycle. In spite of several methods for CO_2 consumption, its electrochemical reduction into a suitable chemical fuel is much promising. But the primary challenges in electrochemical CO_2 reduction deals with the complex reduction kinetics which produce multiple products. In addition, hydrogen evolution reaction always competes with it. Therefore, recent studies focus on the selective CO_2 reduction as well as the control of hydrogen evolution reaction. In this work, we report the enhanced selectivity of the CO_2 reduction at Cu modified diamond electrode in ionic liquid. Firstly, we optimized and deposited fine Cu nanoparticles on diamond substrate and then the suitably deposited Cu-diamond electrode was used as the cathode for electrochemical CO_2 reduction. This Cu modified diamond electrode is found to show higher product selectivity for the formation of CO. In addition, hydrogen evolution reaction can be controlled using this Cu modified diamond electrode. Conductive diamond electrode is one of the stable materials which possesses high potential window for electrochemical reactions with noncorrosive nature. We believe that diamond modification with other suitable materials would be of potential interests for the electrochemists to design a reliable cathode material for CO_2 reduction.

3 Development of diamond photocatalyst for CO_2 reduction

Electrochemical or photoelectrochemical CO_2 reduction generally follows multiple proton coupled electron transfer (MPCET) reaction mechanism which provides poor selectivity. In addition, MPCET goes through many unstable/metastable intermediates thereby the efficiency becomes poor. Though single electron transfer (SET) CO_2 reduction could pave the way of selectivity; CO_{2^-}, an intermediate of this path which requires extremely high energy and thereby the development of the suitable catalysts of this path for efficient CO_2 reduction is still lacking. Herein we report the promotion of SET CO_2 reduction which synergies with silver (Ag) nanoparticles for efficient reduction kinetics. First, the reaction was monitored using a semiconductive boron-doped diamond photoelectrode which transfer high energy electron to CO_2 molecule to form CO_{2^-} intermediate and then this intermediate was stabilized through the interaction with the nearest Ag nanoparticles deposited on diamond photoelectrode. Such synergy effect leads to an almost 3 fold and 50 fold higher CO_2 reduction activity compared to only electrochemical CO_2 reduction on Ag surface or photoelectrochemical SET CO_2 reduction on diamond surface, respectively. This SET CO_2 reduction not only enhances the efficiency and selectivity, but also exhibits a tremendous resistance towards hydrogen evolution reaction in aqueous electrolyte extending the reliability and possibility of SET CO_2 reduction for solar energy conversion and storage.

Development and Applications of Cooperative Catalysts towards Life Innovation

41

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Co-PIs

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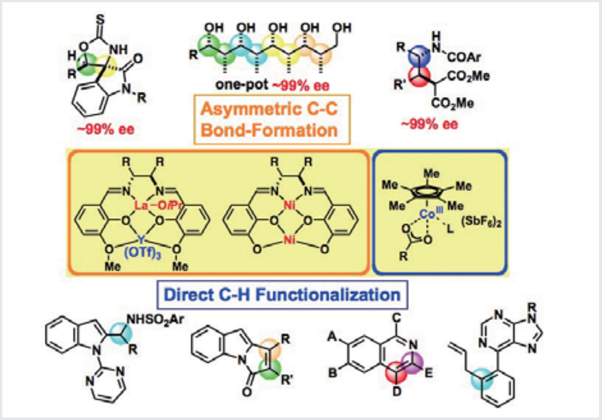
To contribute “Life Innovation” and “Green Innovation”, we developed various new cooperative catalysts. (i) In bimetallic cooperative Schiff base asymmetric catalysts, two metals work simultaneously to promote organic transformations under mild reaction conditions with high stereoselectivity. The synthesis of chiral building blocks useful for design and synthesis of pharmaceuticals were achieved with minimum wastes. (ii) As alternatives to highly reactive but expensive Rh(III)-catalysts, we utilized earth-abundant cobalt and developed catalytically active cationic Co(III)-catalysts. The Co(III)-catalysts were used for the direct catalytic carbon-hyrdogen bond functionalization of indoles, pyrroles, 6-aryl-purines as well as the synthesis of heterocyclic compounds.



1 Application of Two-Center Cooperative Asymmetric Catalysts

We utilized our two-center cooperative asymmetric catalysts for production of unnatural amino acids and spiro-oxindoles bearing tetrasubstituted chiral stereocenters. By the aid of cooperative function of two catalytically active centers, high stereoselectivity and catalytic activity were realized under mild reaction conditions. Careful selection of two metals and fine electronic and steric tuning of each metal center played key roles to maximize the cooperative functions. It is noteworthy that two-center cooperative catalysts promoted target reactions under simple proton transfer manner, thereby the amount of wastes and steps required for the synthesis decreased in comparison with conventional organic transformations. We hope the two-center cooperative asymmetric catalysts will lead more efficient and sustainable process of various chemicals.

2 Development of Cationic Cobalt Catalysts as Alternatives to Precious Rhodium Catalysts

Direct carbon-hydrogen bond functionalization process will contribute to shorten the synthetic routes of useful chemicals and to minimize wastes of each process. For the carbon-hydrogen bond functionalization process, precious metals like rhodium were often used because of their high catalytic activity. When considering the production cost and environmental issues, however, the development of less expensive and earth-abundant metal catalysts as alternatives to precious late transition metal catalysts is highly demanded. To address this issue, we developed cationic high valent cobalt catalysts, Cp*Co(III) catalysts, to replace Cp*Rh(III) catalysts. The Cp*Co(III) catalysts showed high catalytic activity for directed carbon-hydrogen bond functionalization of indoles, pyrroles, and other heterocyclic compounds useful for pharmaceutical production. Computational analysis of the reaction mode of Cp*Co(III) catalysts indicated that cooperative function of a cationic cobalt metal center and an anionic carboxylate unit is important to realize high activity with cobalt metals.

3 Unique Catalytic Activity of First-Row Cobalt Catalysts over Rhodium Catalysts

The Cp*Co(III) catalysts developed in this project not only worked nicely as alternatives to corresponding Cp*Rh(III) catalysts, but also exhibited unique catalytic activity in comparison with Cp*Rh(III) catalysts. High Lewis activity and high reactivity of organocobalt species were utilized for one-pot production of pyrroloindolones, which are versatile cores for the design of biologically active compounds. High oxophilicity of cationic cobalt species was utilized to realize direct dehydrative carbon-hydrogen bond allylation using non-activated free allylic alcohols. The protocol provided useful building blocks just by releasing water as side adducts. Small ionic size of Cp*Co(III) catalysts was also utilized to realize high site selectivity in carbon-hydrogen bond activation steps, which are generally difficult with Cp*Rh(III) catalysts.

Development of Catalytic Asymmetric C-C Bond Forming Reactions for Organofluorine Compounds and Industrial Applications

42

Principal Investigator (PI)

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Co-PIs

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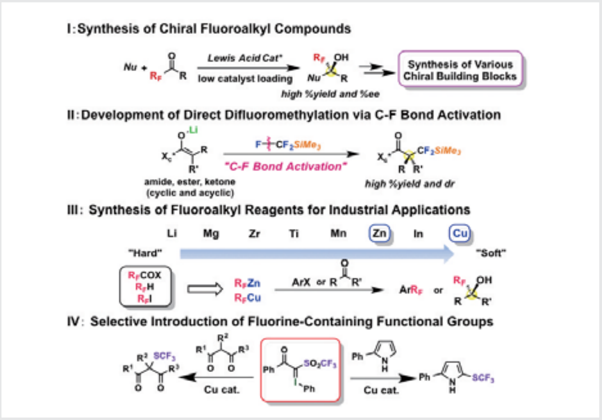
Our project is directed toward the development of practical and industrial synthesis of organofluorine compounds, which attracts current attention in view of their important applications in biological and material science, based on novel catalytic asymmetric carbon-carbon bond forming (CCF) reactions. The novel synthetic methods for various chiral organofluorine compounds by the catalytic asymmetric carbon-carbon bond forming reactions based on inert C-F bond activation will also be developed in this project. The results of our four kinds of research (I ~ IV) are shown.



1 Synthesis of Chiral Fluoroalkyl Compounds

We have succeeded in a variety of catalytic asymmetric carbon-carbon bond forming reactions, such as ene, yne, and Friedel-Crafts (F-C) reactions, with trifluoropyruvate employing chiral dicationic Pd complexes as chiral Lewis acid catalysts. The Pd complexes have been found to be useful as the air- and moisture-stable asymmetric catalysts, which are easily prepared. Especially, the catalytic activity can be retained even by low catalyst loading, and the carbonyl-ene reaction of trifluoropyruvate with isobutene provides a key intermediate (HMTPAE) for biologically active compounds in industrial scale. We have also succeeded in a highly enantioselective and atom-economical [2+2] cycloaddition of diverse array of alkynes with trifluoropyruvate using chiral dicationic Pd catalysts to provide the unprecedentedly stable oxetene derivatives. Recently, we have reported the novel and practical catalytic asymmetric three-component coupling reaction to create molecular diversity from simple and readily available substances; terminal alkyne or alkene, arene, and fluoromethylpyruvate.

2 Development of Direct Difluoromethylation via C-F Bond Activation

We have reported the first examples of C-F bond activation of the Ruppert-Prakash reagent (CF_3TMS) as an electrophile through the polarity inversion to a formal siladifluoromethyl cation ($TMSCF_{2}{}^{+}$). This direct α-siladifluoromethylation of lithium enolate with CF_3TMS proceeded via C-F bond activation and C-C bond formation leading to the construction of the α-siladifluoromethyl-attached quaternary and tertiary carbon centers with high synthetic and biological potential. Additionally, the reaction of carbonyl compounds bearing chiral oxazolidinone auxiliary produced the chiral α-siladifluoromethylated compounds in high diastereoselectivities. Recently, we have also succeeded in the direct α-difluoromethylation of various nitrile compounds with a slight excess amount of *n*BuLi (1.1 equiv) and fluoroform (1.5-2.0 equiv), which is an ideal fluoromethylating reagent, to afford the corresponding α-difluoromethylated products with quaternary carbon center in moderate to high yields. Development of direct catalytic asymmetric difluoromethylations using fluoroform and the Ruppert-Prakash reagent in the presence of chiral transition-metal catalyst is ongoing in our laboratory.

3 Synthesis of Fluoroalkyl Reagents for Industrial Applications

We have succeeded in the direct synthesis of the $CuCF_3$ and CuC_2F_5 reagents from cuprate and ethyl trifluoroacetate and pentafluoropropionate as one of the most useful fluoroalkylating source. Furthermore, these reagents can be successfully applied to two types of trifluoro- and pentafluoro-ethylations with arylboronic acids and aryl bromides to provide the fluoroalkylated aromatic compounds in good-to-excellent yields, respectively. In the case of perfluoro-zinc chemistry instead of copper one, the aromatic perfluoroalkylation catalyzed by copper(I) salt with bis(perfluoroalkyl) zinc reagents $Zn(R_F)_2(DMPU)_2$, which were prepared and then isolated as a stable white powder from perfluoroalkyl iodide and diethylzinc, has been accomplished to provide the perfluoroalkylated products in good-to-excellent yields.

4 Selective Introduction of Fluorine-Containing Functional Groups

In the last few decades, numerous methods for the introduction of a trifluoromethylthio group into organic compounds have been developed. The most attractive and ideal route to constitute the CF_3S moiety is the direct introduction of this functional group. In this context, we have disclosed a novel trifluoromethanesulfonyl hypervalent iodonium ylide as a shelf-stable reagent for electrophilic-type trifluoromethylthiolation. A wide variety of nucleophiles are nicely converted into the corresponding trifluoromethylsulfanyl products by this reagent.

Development of CO_2 Photo-Reduction System Based on Semiconductor Quantum-dots Photocatalyst.

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Principal Investigator (PI)

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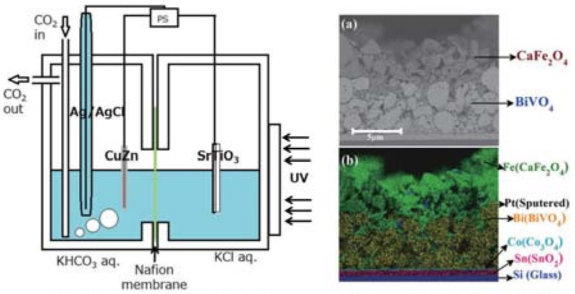
Tokyo Institute of Technology

This project aims to develop a CO_2 photo-reduction system based on semiconductor photocatalysts. To achieve the efficient CO_2 photo-reduction reaction, we propose the two important requirements; 1) development of efficient cocatalyst to drive multi electron reduction by an electrochemical investigation under dark condition, 2) modification of these cocatalysts onto effective light harvesters to cause photocatalytic CO_2reduction. We developed the Cu-Zn intermetallic as an effective cocatalyst to drive CO_2 reduction for fuel production. The Cu-Zn intermetallic nanoparticles are combined with visible light harvester, such as Cu_2ZnSnS_4 and $CaFe_2O_4$, then we construct the photoelectrochemical or Z-scheme artificial leaf device.



Photoelectrochemical system

Artificial Z-scheme leaf device

1 Cu-Zn intermetallic cocatalyst for CO_2 reduction

Our group previously reported copper oxide nanocluster with mixed valence number as an effective cocatalyst to drive CO_2 reduction (*ACS Nano*, 9, 2111, 2015). Based on the previous research, we proposed the copper based intermetallic would be more active cocatalyst. Synthesis for thin film or nanoparticles of copper based intermetallic has been established. According to our exploration on various intermetallic composition, Cu-Zn was very effective cocatalyst to reduce CO_2 into formic acid. Cu-Zn is composed of ubiquitous element and can be facilely synthesized, thus this intermetallic is one of the best cocatalysts to drive CO_2 reduction.

2 Combination of Cu-Zn cocatalyst onto $SrTiO_3$ light harvester

The Cu-Zn intermetallic film was used as a cathode, while mesoporous $SrTiO_3$ electrode was used as a photoanode, then the UV light was irradiated on $SrTiO_3$ side. And as a result, formic acid was formed in electrolyte solution, while carbon monoxide was produced at the head space of a reactor even in the absence of any bias application. Selectivity for formic acid formation was very high and its Faradaic efficiency was 65 %, according to the consideration on the photocurrent density under rest potential condition. We also developed Cu-Zn intermetallic nanoparticles and deposited them onto $SrTiO_3$ powder. Photocatalytic CO_2 reduction was also confirmed in the powder system, and isotope experiment proved the origin of the product was CO_2. However, the Cu-Zn and $SrTiO_3$ system only utilizes UV light, thus we try to combine the Cu-Zn intermetallic with visible light harvester, such as a Cu_2ZnSnS_4 photocathode. Further the developed photocathode will be combined with Fe_2O_3 or WO_3 photoanode to construct the Z-scheme CO_2 photoreduction system, which is driven by visible light irradiation.

3 Z-scheme artificial leaf device

Heterogeneous bilayered semiconductor thin films were fabricated using p-type $CaFe_2O_4$ and n-type $BiVO_4$ for photocatalytic overall water splitting (*ACS Catal.* 6, 2197, 2016). The interface of the semiconductor layers was modified with Co_3O_4 as oxidation cocatalyst and Pt as reduction cocatalyst. The resulting a bulk heterojunction film, which was composed of $Co_3O_4/BiVO_4/Pt/CaFe_2O_4/Pt$, produced both oxygen and hydrogen under visible-light irradiation in the absence of applied bias potential or sacrificial agents. Thereby it generated H_2 and O_2 molecules in a 2:1 stoichiometric ratio, indicating overall water splitting under visible light irradiation. We introduce the Cu-Zn intermetallic layer at the photocathode interface to cause CO_2 photoreduction, which will be driven under visible light in the absence of applied bias potential.

Creation of Azoles-Based Orthographic π-Electron Molecules via Development of New Synthetic Reactions

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Principal Investigator (PI)

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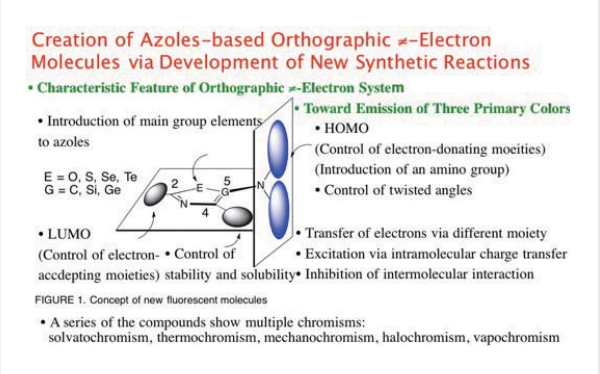
Professor, Gifu University

New compounds showing blue, green and red fluorescence are provided by the combination of starting materials consisted with readily available elements. For this purpose, the following our own original idea was proposed, i.e., molecules possess unique steric structures. In addition, to achieve the construction of the molecules, new catalytic reactions are also developed.



Creation of Azoles-based Orthographic ≠-Electron Molecules via Development of New Synthetic Reactions

- Characteristic Feature of Orthographic ≠-Electron System

- Introduction of main group elements to azoles

E = O, S, Se, Te
G = C, Si, Ge

- Toward Emission of Three Primary Colors
- HOMO
(Control of electron-donating moeities)
(Introduction of an amino group)
- Control of twisted angles
- LUMO
(Control of electron-accdepting moieties)
- Control of stability and solubility
- Transfer of electrons via different moiety
- Excitation via intramolecular charge transfer
- Inhibition of intermolecular interaction

FIGURE 1. Concept of new fluorescent molecules

- A series of the compounds show multiple chromisms:
solvatochromism, thermochromism, mechanochromism, halochromism, vapochromism

1 Comprehensive Synthesis of 5-N-arylaminothiazoles

By using the chemical species derived from powdered sulfur, arylmethylamines, aromatic amines as key species, 5-N-arylaminothiazoles, whose core structures are pentagon-shaped are provided for the first time all over the world. The compounds have three positions where a range of substituents are introduced, and in fact the library of the compounds more than 70 is constructed. The substituents whose introductions are hard by ordinary transition metal-catalyzed reactions, such as pyridyl, hydroxy and alkylthio groups are introduced. Furthermore, alkynyl and azido groups, which can be used as linkers in the click reactions to biomolecules are attached. Hydroxy, thio, and pyridyl groups are used as anchors, and with these functional groups, the extension of π-electrons is achieved. The coordination of those to Lewis acids and metals also leads to new derivatives. Despite the fact that electron-donating and –withdrawing groups in a series of compounds are highly three-dimensionally deviated, they show rather strong fluorescence and show solubility toward nonpolar and polar solvents.

2 Fluorescent spectra and electrochemical properties of 5-N-arylaminothiazoles

Comprehensively synthesized 5-N-arylaminothiazoles show fluorescence from blue to orange depending on the substituents to the 2- and 5-positions of 5-N-aryaminothiazoles With these properties, their unique photophysical, electrochemical properties and molecular structures were disclosed. For example, the absorption spectra were consistent in different solvents, whereas solvatochromism was observed for fluorescent spectra. In fact, the fluorescence spectra in more polar solvents showed red-shifts. On the basis of the relationship between the parameters of polarities and difference of the energies of absorptions and emissions, the structural change of ground and excited states was estimated. As a result, the molecules became more polar in the excited states. The electrochemical oxidation and reduction were also carried out. The results showed the compounds showed reversible one-electron oxidation wave. The introduction of electron-donating groups to the substituents on the nitrogen atom at the 5-position reduced oxidation voltage, and the introduction of the dimethylamino group exhibited two-electron oxidation wave.

3 C-H functionalization of imidazoles by using cationic nitrogen-containing bidentate Pd catalysts

The reactivity of the carbon-halogen bonds (C-X bonds) toward transition metal complexes is generally higher that of the carbon-hydrogen bonds (C-H bonds). In this regards, to introduce three different substituents to imidazoles with two bromine atoms and one hydrogen atom, the processes to selectively cleave C-H bonds in the initial step followed by the sequential but selective cleavage of C-X bonds were aimed. As a result, cationic Pd complexes with phenantrolines as a ligand, which were developed by us, was found to perform selective cleavage of C-H bonds followed by the introduction of a range of aromatic groups having electron-donating and –withdrawing groups to that carbon atom. Further transformation of the resulting imidazoles with two bromine atoms and one aromatic group was successfully carried out. With these sequential processes, the compound showing anti-allergy effect was provided.

Development of Solar-Driven Molecular Transformations

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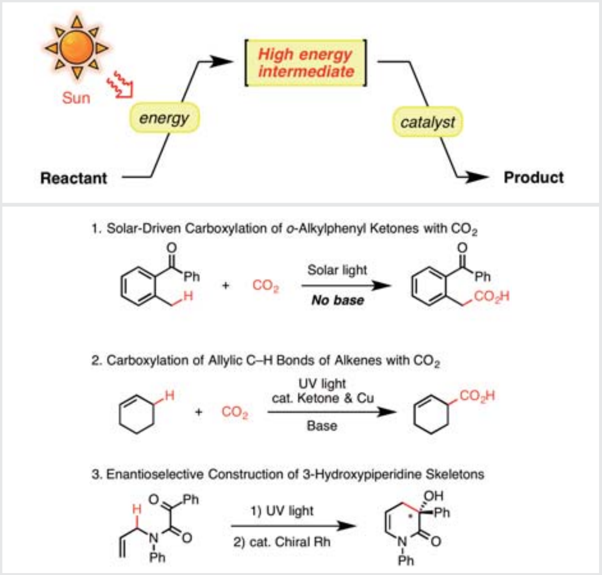
Principal Investigator (PI)

Masahiro MURAKAMI
Professor, Graduate School of Engineering, Kyoto University

The modern society has been mainly based on the energy derived from fossil fuels. However, issues of global warming and the depletion of fossil fuels have incited a strong demand for exploration of innovative means to exploit energy from sustainable sources. Synthetic chemists can contribute by developing new synthetic methods utilizing sunlight, which is undoubtedly the best source of sustainable energy available on the planet. In this project, we aim at the development of new C–C bond forming reactions that exploit solar light as the energy source.



1 Solar-Driven Carboxylation of o-Alkylphenyl Ketones with CO_2

CO_2 is thermodynamically stable. Consequently, most of conventional C–C bond forming carboxylation reactions with CO_2, including the novel methods based on transition metal catalysis, requires highly energetic reagents like Grignard reagents and manganese(0) metal. The major driving force of these carboxylation reactions derives from the highly energetic chemical reagents. Alternatively, electro- or photo-assisted reductive carboxylation reactions have been devised. Electron donors like triethylamine were used as the sacrificial reducing agents in most cases. In this project, we found a unique and clean carboxylation reaction which uses no sacrificial reagent but only light energy as the driving force; simply upon UV irradiation of a DMSO solution of *o*-alkylphenyl ketones, CO_2 is efficiently incorporated to produce *o*-acylphenylacetic acids. The present carboxylation reaction provides a simple and straightforward access from readily available materials (*o*-alkylphenyl ketones, CO_2, and hydrazine) to 2,3-benzodiazepines, which constitute a versatile pharmacophore of various biologically active compounds including Tofisopam and Girisopam.

2 A Light/Ketone/Copper System for Carboxylation of Allylic C–H Bonds of Alkenes with CO_2

Alkenes are readily available and abundant chemical feedstock. The C–C bond forming carboxylation reactions of alkenes with CO_2 would be highly attractive as the fundamental synthetic technology for the preparation of polyesters and polyamides. However, such a carboxylation reaction is quite challenging because both alkenes and CO_2 are not so reactive, even in the presence of a catalyst. In this project, we found that an allylic C–H bond of simple alkenes is directly carboxylated with CO_2 in the presence of a substoichiometric amount of a ketone and a catalytic amount of a copper complex under UV irradiation. The unique carboxylation reaction proceeds through a two-stage mechanism consisting of an endergonic photoreaction of ketones with alkenes forming homoallyl alcohol intermediates and a thermal copper-catalyzed allyl transfer reaction from the homoallyl alcohols to CO_2 through C–C bond cleavage.

3 Enantioselective Construction of 3-Hydroxypiperidine Skeletons by Sequential Actions of Light and Rhodium on *N*-Allylglyoxylamides

A 3-hydroxypiperidine skeleton is one of the structural motifs frequently found in biologically active compounds. Although a wide variety of methods have been developed for construction of piperidine skeletons, there is still a demand for catalytic asymmetric procedures for 3-hydroxypiperidines with a quaternary carbon center at the 3-position. In this project, we developed a method to construct 3-hydroxypiperidine skeletons in a highly enantioselective manner (96-98%ee) starting from *N*-allylglyoxylamides, which are readily prepared from commercially available starting materials (glyoxylamides, anilines and allyl bromide); sequential actions of UV light and a chiral rhodium catalyst upon *N*-allylglyoxylamides gave rise to the piperidine skeleton. In a formal sense, the allylic C–H bond of the *N*-allylamide is selectively cleaved and added across the ketonic carbonyl group with migration of the double bond (carbonyl-ene type reaction) to construct the six-membered ring with formation of a chiral quaternary carbon center in an atom-economical way.

Development of Photocatalysts for Solar CO_2 Reduction Utilizing H_2O as an Electron Donor and a Proton Source

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Principal Investigator (PI)

Takeshi MORIKAWA
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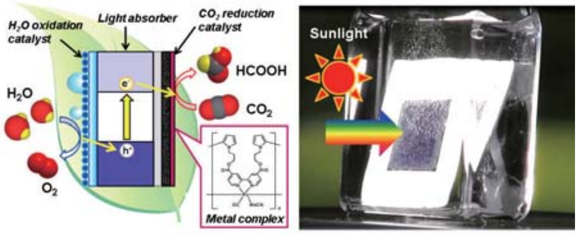
Morikawa Senior Fellow Lab.,
Toyota Central Research and Development Labs., Inc.

We have been developing a highly efficient artificial-photosynthetic system operating under solar irradiation, which produces C1-chemicals from CO_2 using H_2O as an electron donor and a proton source without any external electrical bias. We have constructed hybrid photocatalysts composed of semiconductors and metal-complex catalysts, and demonstrated a solar-to-chemical conversion efficiency for formate generation exceeding those of plants. Our next target is to construct the semiconductors/metal-complex system composed of earth-abundant elements only, and to realize electroccatalysts to generate larger molecules such as alcohols.



1 A monolithic device with solar-to-chemical conversion efficiency of 4.6%

A monolithic tablet-shaped device for the artificial photosynthetic reaction, which is composed of IrO_x as a water oxidation catalyst, carbon/Ru-polymer as a CO_2 reduction catalyst, and Si-Ge heterojunction as a light absorber, was constructed. This "artificial leaf" produced formate in phosphate buffer aqueous solution containing CO_2 with a solar conversion efficiency of 4.6 % (change in Gibbs free energy), which exceeded those of plants without any external assists. By isotope tracer analyses, carbon and proton sources for formate formation were confirmed to be from CO_2 and H_2O molecules, respectively.

2 CO_2 photoreduction using p-type Fe_2O_3 coupled with Ru-complex

A *p*-type semiconductor composed of earth-abundant elements, N,Zn-codoped Fe_2O_3, was utilized for photoelectrochemical CO_2 reduction under solar simulated light irradiation. The reaction rate was significantly improved by constructing a multi-heterojunction with oxides and surface-immobilization of a Ru complex polymer catalyst. Unassisted and stoichiometric CO_2 reduction coupled with the water oxidation reaction through the use of this iron-based photocathode was also demonstrated by connection with a photoanode with a solar-to-chemical energy conversion efficiency of 0.15%.

3 Challenge for a powdered solar CO_2 reduction system

A powdered Z-scheme system for the photocatalytic water splitting reaction under visible light irradiation was successfully demonstrated utilizing a combination of a Ru-complex catalyst for CO_2 reduction, $SrTiO_3$:Rh as a photoabsorber for electron transfer to the Ru-complex, $BiVO_4$ as a water oxidation photocatalyst, and reduced graphene oxide (RGO) as an electron mediator between the semiconductors. Stoichiometric generation of H_2 and O_2 were confirmed, which suggested complete water splitting reaction was conducted. It was also speculated that hydrogen was generated instead of C1 chemicals over the Ru-complex due to inefficient electron transfer to the complex in a total system. Professor Akihiko Kudo at Tokyo University of Science has been supporting the work on powdered system.

Fundamentals of Self-Contact Organic Transistors

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Principal Investigator (PI)

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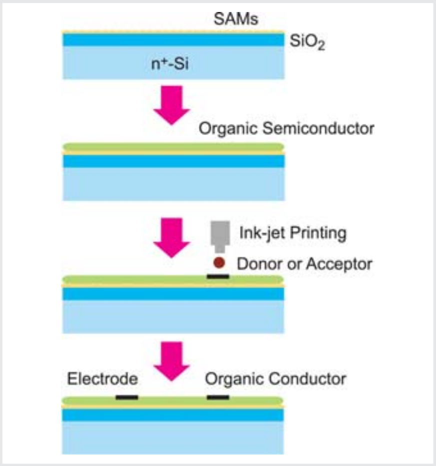
Department of Materials Science and Engineering

π-Electron systems play a principal role in organic electronics as organic semiconductors, but also work as organic electron donors and acceptors to form highly conducting charge-transfer complexes upon chemical doping. In the present project, by using selectively patterned doping and a printing method, the active layer as well as the electrode parts are formed from the same organic material, which is used as an organic semiconductor and an organic conductor at the same time to achieve all-organic electronics.



1 Development of self-contact organic transistors

"Self-contact organic transistors" are developed, where the organic semiconductor film is selectively doped, and the resulting highly conducting organic charge-transfer salt is used as the electrode part. The chemical doping is achieved by the evaporation method as well as the solution method using the inkjet printing. Since the electrode part is made from an organic material, the substrate and the gate dielectric are also fabricated by using organic materials, and "all organic transistors" showing the mobility of more than 1 cm^2/Vs are realized. Chemical doping to representative organic transistor materials is attempted, and a new type of organic charge-transfer salts with very high conductivity are obtained. These findings open a new possibility of organic electronics using chemical doping.

2 High-performance ambipolar organic transistors

Ambipolar organic semiconductors capable of both electron and hole transport have attracted considerable attention, where ambipolar semiconductors are usually realized using donor-acceptor polymers. We have explored small-molecule ambipolar semiconductors, and developed indigo derivatives which exhibit electron and hole mobilities of nearly 1 cm^2/Vs. We have also developed small-molecule ambipolar materials based on isoindigo, binaphthyl compounds, and diketopyrrolopyrrole derivatives. These units are promising moieties in donor-acceptor polymers with potential application to organic solar cells and light-emitting transistors.

3 Band-like transport down to low temperatures in organic transistors

It has been known that some organic charge-transfer complexes show metallic conductivity down to low temperatures, and high-quality organic-semiconductor crystals show band-like transport down to low temperatures, where the mobility measured by the time-of-flight method increases. However, it has been a great challenge to achieve organic transistors showing band-like transport down to low temperatures. We have demonstrated as-grown single-crystal transistors of benzothienobenzothiophene exhibit band-like transport even below 100 K. The four-probe mobility continues to increase to more than 150 cm^2/Vs. Our transistors show an anomaly around 80 K, but we have achieved transistors that do not turn to the hopping transport down to helium temperatures.

Development of Advanced Catalytic Systems with Dimensionally-Regulated Nano Spaces and Heterogeneous Accumulated Transition Metal Nano Catalysts for the Production of π-Electron Molecules

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Principal Investigator (PI)

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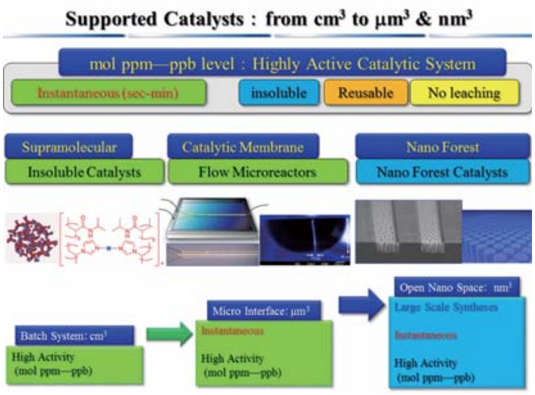
Co-PI

Shigenori FUJIKAWA
Associate Professor, International Institute for Carbon-Neutral Energy Research, Kyushu University

Our aim for the research is the development of advanced insoluble/heterogeneous metal catalytic systems that produce the desired organic molecules with mol ppm-ppb amount of the catalysts with high reusability for low-energetic, environmentally benign and sustainable molecular transformation. For this purpose, we propose the following themes to develop catalytic systems for the synthesis of pi-molecules with high catalytic activity, reusability and selectivity; (1) development of supramolecular polymeric metal catalysts of non-crosslinked polymers and metal species that should work with mol ppm-ppb amount; (2) preparation of catalytic membrane-installed flow reactor systems that should provide instantaneous organic transformations; (3) creation of catalyst-installed nano forest reactors that should works with mol ppm-ppb amount.



1 Development of Insoluble Supramolecular Polymeric Palladium Catalysts

Several mol % of homogeneous palladium catalysts are used for cross-coupling reactions generally. It is difficult to recover the catalysts that easily contaminate the products. We developed an insoluble supramolecular polymeric palladium catalyst of an amphiphilic polymeric imidazole and palladium species. By using less that one mol ppm to several mol ppm Pd of the catalyst, the Suzuki-Miyaura reaction, allylic arylation and the Mizoroki-Heck reaction proceeded efficiently to give the corresponding products in high yield. The catalyst was readily recovered and reused without loss of catalytic activity. No palladium leaching to the products was not detected. The catalyst should be applied to the efficient synthesis of pharmaceutical and functional chemicals with lower cost.

2 Development of Catalytic Polymeric Copper Membrane-immobilized Microflow Device

Microflow reactors as flow reaction system are paid attention to for the new generation green chemistry. It is possible to form liquid-liquid laminar flows inside a microflow reactor. We developed polymeric metal catalytic membrane-immobilized microflow reactors by preparing the membranes at the interface of two laminar flows for the first time. For example, we prepared a polymeric copper membrane-installed microflow reactor that promoted Huisgen cycloaddition, an important reaction for click chemistry, within a few to several ten seconds. It should be applied to the synthetic systems that require instantaneous transformations such as the synthesis of PET medicals.

3 Development of a Silicon Nanoforest Catalytic Reactor

We created advanced catalytic systems with dimensionally-regulated nano spaces and heterogeneous accumulated transition metal nano catalysts. We controlled the chemical structure of transition metal catalysts and the dimension of catalytic reaction spaces to provide insoluble catalytic synthetic systems, catalytic membrane-installed microflow instantaneous reaction systems, and 3D nano-pinholder space -controlled instantaneous reaction systems (nano forest reactor) with high catalytic activity. Thus, we developed a new platform for the catalytic reactions, a silicon nanowire array-stabilized palladium nanoparticle catalyst, SiNA-Pd. The novel device was applied to the Mizoroki-Heck reaction, the hydrogenation of an alkene, the hydrogenolysis of nitrobenzene, the hydrosilylation of an α,β-unsaturated ketone, and the C-H bond functionalization reactions with high catalytic activity and reusability.

The silicon nanowire array-stabilized Pd nanoparticle catalyst SiNA-Pd was applied to the C-H bond functionalization. The reaction of iodobenzene and 2-methylthiophene afforded 2-methyl-5-phenylthiophene in 80% yield. The hydrogenation of stilbene, the hydrogenolysis of nitrobenzene, and the hydrosilylaton of 2-benzylpropenal gave the corresponding products in high yield. SiNA-Pd with 490 mol ppb Pd (0.000049 mol % Pd) was applied to the reaction of the 10-gram scale substrate to give butylcinnamate in 95 % yield, where the turnover number (TON) and turnover frequency (TOF) were 2,000,000 and 40,000 h^{-1}, respectively. An antiasthmatic agent Ozagrel was prapared through the SiNA-Pd-catalyzed Mizoroki-Heck reaction (490 mol ppb Pd).

Design of Molecular Acid Catalyst

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Principal Investigator (PI)

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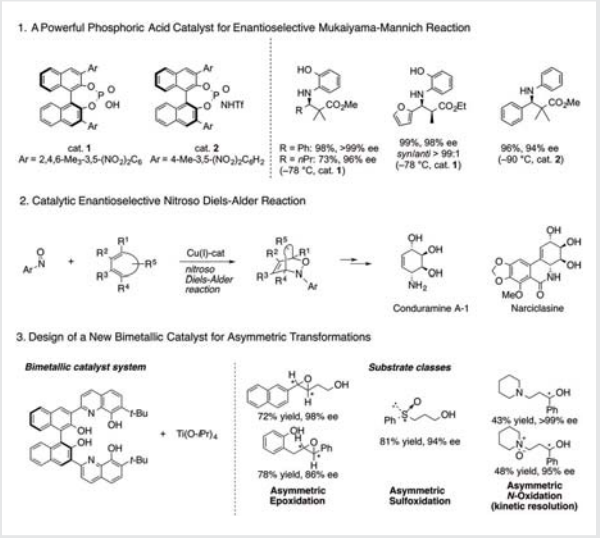
Co-PI

Matsujiro AKAKURA
Associate Professor, Aichi Educational University

Enzyme is a giant molecule widely distributed in biological system, which is a crucial catalyst for making various biologically important molecules in living systems. It was known that the true man-made mimics of these enzymes, "chemzymes" are exceedingly difficult to design and prepare. The aim of the present project is to design and synthesis of truly useful chemzymes. Specifically, new Lewis and Brønsted acid catalysts will be prepared and use them as synthetic catalysts for various chemical transformations, especially for asymmetric pathways to new carbon-carbon bond formations.



1 A Powerful Phosphoric Acid Catalyst for Enantioselective Mukaiyama-Mannich reaction

A new chiral phosphoric acid bearing 2,4,6-trimethyl-3,5-dinitrophenyl substituent at the 3,3′-position (cat. **1**) has been developed. The utility of this catalyst was demonstrated by a highly enantioselective and diastereoselective asymmetric Mukaiyama-Mannich reaction of imines with a wide range of ketene silyl acetals. Moreover, this method was successfully applied to the construction of vicinal tertiary and quaternary stereogenic centers in excellent enantioselectivities and diastereoselectivities. Significantly, *N*-triflyl phosphoramide (cat. **2**) presents a complementary catalyst system for this type of chemistry in terms of more challenging imines without 2-hydroxyphenyl moiety.

2 Catalytic Enantioselective Nitroso Diels-Alder Reaction

The nitroso Diels–Alder (NDA) reaction is an attractive strategy for the synthesis of 3,6-dihydro-1,2-oxazines and 1-amino-4-hydroxy-2-ene derivatives. Herein we report the Cu(I)–DTBM-Segphos catalyzed asymmetric intermolecular NDA reaction of variously substituted cyclic 1,3-dienes using highly reactive nitroso compounds derived from pyrimidine and pyridazine derivatives. In most of the cases studied, the cycloadducts were obtained in high yields with very high regio-, diastereo-, and enantioselectivities. As an application of this methodology, formal syntheses of conduramine A-1 and narciclasine were accomplished.

3 Design of a New Bimetallic Catalyst for Asymmetric Transformations

We have designed a new tethered 8-quinolinol-based ligand, which was developed to obtain the required binuclear titanium complex that efficiently catalyzes the regio- and stereoselective epoxidation of primary and tertiary homoallylic alcohols, as well as first examples of 2-allylic phenols. The new catalyst system also promotes the asymmetric oxidation of γ-hydroxypropyl sulfides and γ-amino alcohols giving an important class of hitherto inaccessible chiral sulfoxides and *N*-chiral amine oxides.

Construction of New π-Electron Systems by Aromatic Fusion Reactions Utilizing Arynes

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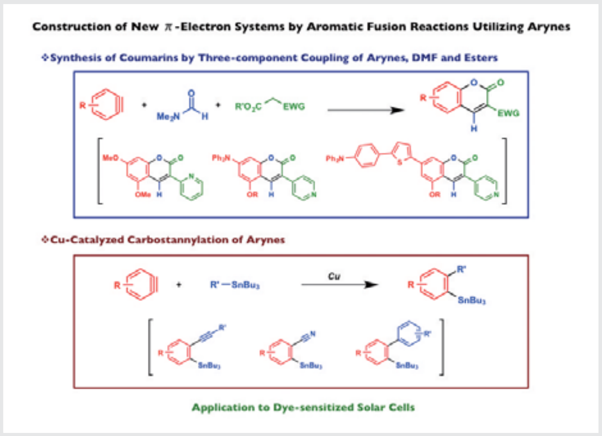
Principal Investigator (PI)

Hiroto YOSHIDA

Associate Professor, Graduate School of Engineering,
Hiroshima University

This project aims at developing new reactions with reactive intermediate arynes bearing a strained carbon–carbon triple bond, which provide efficient methods for synthesizing a variety of aromatic π-electron systems. With this approach, newly constructed π-electron systems can be fused with aromatic rings of arynes to give expanded π-electron systems, which will be utilizable for functional materials.



Construction of New π-Electron Systems by Aromatic Fusion Reactions Utilizing Arynes

❖Synthesis of Coumarins by Three-component Coupling of Arynes, DMF and Esters

❖Cu-Catalyzed Carbostannylation of Arynes

Application to Dye-sensitized Solar Cells

1 Three-component coupling of arynes for synthesizing coumarins

We have already developed a new three-component coupling reaction of arynes, DMF and esters (or nitriles) bearing an active methylene moiety that produces coumarins in a straightforward manner. The three-component coupling should proceed through initial formation of an *ortho*-quinone methide, generated by formal [2+2] cycloaddition between a triple bond of an aryne and a carbonyl moiety of DMF. Subsequent [4+2] cycloaddition between the *ortho*-quinone methide and an *in situ*-generated ester enolate, followed by elimination of an alkoxide and dimethylamine furnishes a coumarin. Since the generation of an ester enolate via facile deprotonation is the key for the successful three-component coupling reaction, a variety of active methylene compounds of high acidity including malonates, β-ketoesters, pyridylacetates, etc. could participate in the reaction to give the respective coumarins with high efficiency. Because the present method enables *ortho*-quinone methides acting as powerful 4π components to be generated efficaciously, a variety of benzo-fused six-membered rings should be accessible via the [4+2] cycloadditions with other 2π components than enolates.

2 Synthesis of coumarin dyes and their application to DSSCs

We have found that the reaction was also applicable to ethyl 4-pyridylacetate, allowing a pyridyl group, which can serve as an acceptor and an anchoring group, to be installed at 3 position of the coumarin ring. The use of 3-alkoxy-5-chlorobenzyne precursors in the reaction with ethyl 4-pyridylacetate led to the regioselective formation of 3-pyridyl-7-chlorocoumarin derivatives in high yield. The carbon–chlorine bond of the coumarins thus obtained were found to be convertible into a carbon–nitrogen bond via the Pd-catalyzed Buchwald–Hartwig coupling reaction with such diarylamines as diphenylamine, 4,4'-di-*tert*-butyldiphenylamine and phenothiazine to afford donor (diarylamine)/acceptor (pyridine)-substituted coumarins, being promising dyes for dye-sensitized solar cells. Moreover, introduction of an aryl–thienyl moiety between the diarylamino moiety and the coumarin unit was also feasible by treatment of 3-pyridyl-7-chlorocoumarin with 5-[4-(diphenylamino)phenyl]-2-thienylstannane under the Migita–Kosugi–Stille coupling conditions, expanding the π-conjugation in the coumarin dye. Actually, the solar energy-to-electricity conversion yield of DSSCs based on these donor/acceptor-substituted coumarin dyes were 1.44% (diphenylamino moiety as donor) and 2.51% (5-[4-(diphenylamino)phenyl]-2-thienyl moiety as donor), demonstrating the promising properties of the coumarins as organic dye sensitizers.

3 Copper-catalyzed carbostannylation of arynes

We have also developed a copper-catalyzed aryne insertion reaction into a carbon–tin bond of alkynylstannanes (carbostannylation). A variety of alkynylstannanes bearing alkylethynyl, arylethynyl and enynyl moieties were found to smoothly undergo the insertion of arynes under the copper catalysis to furnish diverse *ortho*-alkynylarylstannanes in a straightforward manner. The resulting *ortho*-alkynylarylstannanes should be potential intermediates for synthesizing new π-electron systems, because the carbon–tin bond and the carbon–carbon triple bond are utilizable for extending π-conjugation. In addition, the reaction of 4-(diphenylamino)phenylethynyltin with 3-methoxy-4-chlorobenzyne took place with perfect regioselectivity to provide the carbostannylation product having the 4-(diphenylamino)phenylethynyl unit at the *para* position of the chloro group, which can be transformed into a donor/acceptor-substituted extended π-electron system by introducing a pyridyl group through the Pd-catalyzed cross-coupling of the carbon–chlorine bond. The copper-catalyzed carbostannylation of arynes was found to be also applicable to cyanostannane to afford *ortho*-cyanoarylstannanes in high yield, and furthermore arynes could facilely be inserted into a C(sp^2)–Sn bond of arylstannanes.

Catalytic Construction of Nitrogen-Embedded Triply-Fused π-Electronic Systems

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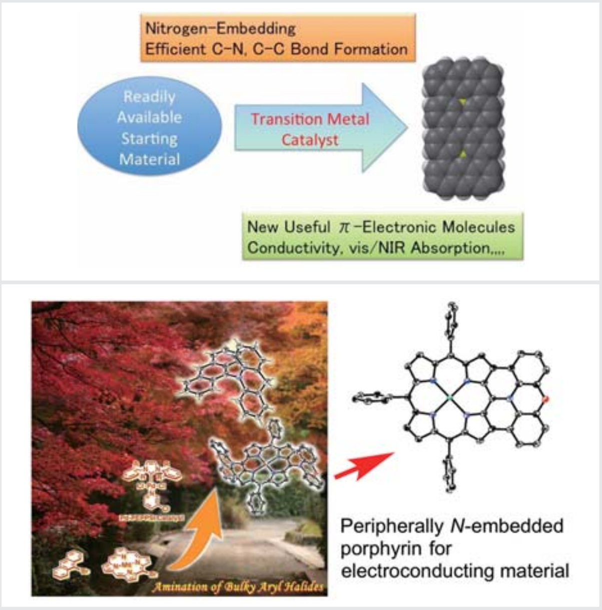
Principal Investigator (PI)

Hideki YORIMITSU
Professor, Department of Chemistry,
Graduate School of Science, Kyoto University

Nitrogen-containing planar π-electronic molecules play key roles in the development of organic electronics such as organic solar cells, organic electroluminescence, and nonlinear optical materials. This project aims at creating new efficient processes for synthesizing useful nitrogen-embedded triple-fused π-electronic molecules with the aid of transition metal catalysis. We sincerely hope that this project will eventually contribute to significant progresses of low carbon technology as well as of organic electronics.



Peripherally *N*-embedded porphyrin for electroconducting material

1 Peripheral Amination of Large π-Conjugated Systems Catalyzed by a Palladium–Carbene Complex

Since triarylamines have found wide applications in organic materials science including OLED and organic solar cells, efficient amination reactions are extremely important tools. Althoug many amination reactions are well known for small or medium-sizedπ-conjugated systems, peripheral aminations of large π-conjugated systems, our target molecules, are still difficult. That strongly drove us to develop a new amination technology by taking advantage of the high catalytic activity of a palladium-carbene complex. We indeed succeeded in synthesizing peripherally aminated large π-conjugated systems, the important precursors of our target molecules, by using a commercially available yet state-of-the-art Pd-PEPPSI-IPr precatalysts. This amination is wide in scope and porphyrins and anthracenes could participate in the amination. We are convinced that Pd-PEPPSI-IPr complexes would be the first choice for amination, and should be applicable to the synthesis of various nitrogen-containing molecules.

2 Oxidative Fusion Reactions of Peripherally Aminated Large π-Conjugated Systems to Prepare Nitrogen-Embedded-Conjugated Systems

We then tried to oxidize peripherally aminated large π-conjugated systems for coplanarization. After numerous attempts, we finally found conditions to successfully obtain novel peripherally nitrogen-embedded porphyrins with high planarity. X-ray crystallographic analysis helped unambiguously determining the structure of one of the porphyrin molecules, which is totally flat. Interestingly, the flat molecule tends to aggregate through planar π-rich network. This assembling tendency would be helpful for smooth intermolecular electron transport. In addition, due to the embedded nitrogen atom bearing a lone pair, the efficiency of electron input/output from the molecule has proved to be significantly enhanced, which is a very favorable property for functional organic electronic materials. This is the first example of coplanarization of π-conjugated systems that are composed of two π-conjugated units and amine-nitrogen, which should be sensitive to oxidation. After this report, many groups are following our method, which clearly indicate the importance and the originality of this protocol.

3 One-step, Transition-Metal-Catalyst-Free Synthesis of Nitrogen-Embedded-Conjugated Systems

As shown above, our groups have reported oxidative fusion reactions of peripherally aminated large π-conjugated systems to prepare nitrogen-embedded-conjugated systems. However, we suffered from multistep syntheses and considerably low yields due to oxidative decomposition of the final products as well as the starting materials. To avoid oxidative coplanarization reactions, we tried to invent an alternative strategy. Beyond our expectation, treatment of large π-conjugated systems that have three halogen atoms in proper positions with diphenylamine in the presence of a strong base resulted in the one-step synthesis of nitrogen-embedded-conjugated systems with remarkably high efficiency. The important feature of this reaction is that this is free from transition metal catalysts. This method is by far the better strategy than the initially designed catalytic method from viewpoints of reaction efficiency, atom economy, pot economy, reaction time, purification, amount of waste, and element strategy, and is regarded as the ultimate way to prepare nitrogen-embedded-conjugated systems.

ACT-C

Advanced Catalytic Transformation program for Carbon utilization

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