Symposium | Asian International Symposium : Asian International Symposium - Electrochemistry -

Fri. Mar 28, 2025 9:00 AM - 11:40 AM JST | Fri. Mar 28, 2025 12:00 AM - 2:40 AM UTC [A]D302(D302, Bldg. 4, Area 3 [3F])

[[A]D302-3am] Asian International Symposium - Electrochemistry -

Chair, Symposium organizer: Shinsuke Inagi, Shintaro Okumura, Yohei Okada, Mugen Yamawaki, Yousuke Ooyama, Toshiki Nokami

9:00 AM - 9:05 AM JST | 12:00 AM - 12:05 AM UTC

Opening Remarks

English Keynote Lecture

9:05 AM - 9:35 AM JST | 12:05 AM - 12:35 AM UTC

[[A]D302-3am-01]

Functional Small Molecules via Synthetic Electrochemistry

○Keyin Ye[1] (1. Fuzhou University, China)

English Invited Lecture

9:35 AM - 9:55 AM JST | 12:35 AM - 12:55 AM UTC

[[A]D302-3am-02]

Electroorganic Synthesis with a Catalytic Amount of Electrical Input

○Eisuke Sato[1] (1. Okayama University)

English Invited Lecture

9:55 AM - 10:15 AM JST | 12:55 AM - 1:15 AM UTC

[[A]D302-3am-03]

Electrochemical single-carbon insertion via distonic radical cation intermediate

○Naoki Shida[1,2] (1. Yokohama National University, 2. JST PRESTO)

10:15 AM - 10:25 AM JST | 1:15 AM - 1:25 AM UTC

Break

Japanese Invited Lecture

10:25 AM - 10:45 AM JST | 1:25 AM - 1:45 AM UTC

[[A]D302-3am-04]

Moderately Oxidizing Thioxanthylium Organophotoredox Catalyzed Radical Cation Cycloaddition Reactions

○Kenta Tanaka[1] (1. Okayama Univ., Research Institute for Interdisciplinary Science)

Japanese Invited Lecture

10:45 AM - 11:05 AM JST | 1:45 AM - 2:05 AM UTC

[[A]D302-3am-05]

Flow Microreactor-Based Selectivity Control of Electrochemical Reactions

○Yosuke Ashikari[1] (1. Hokkaido Universithy)

English Keynote Lecture

11:05 AM - 11:35 AM JST | 2:05 AM - 2:35 AM UTC

[[A]D302-3am-06]

Electrochemistry Opens New Possibilities in Catalytic Alkene Functionalization

○Hyunwoo Kim[1] (1. Pohang University of Science and Technology (POSTECH))

11:35 AM - 11:40 AM JST | 2:35 AM - 2:40 AM UTC

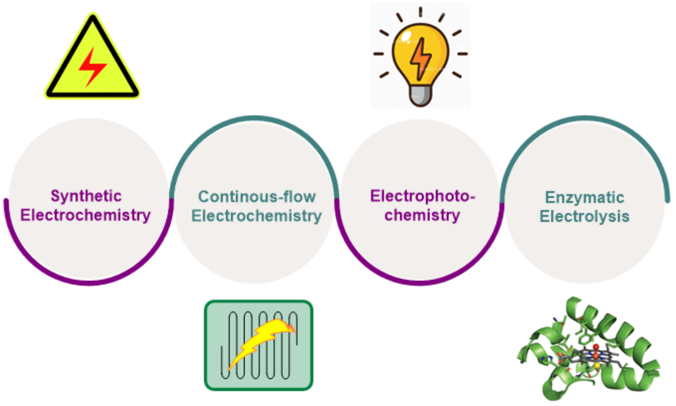
Closing Remarks

Functional Small Molecules via Synthetic Electrochemistry

([1] *College of Chemistry, Fuzhou University, China*) ○Keyin Ye[1]

Keywords: Synthetic Electrochemistry, Oxidation, Scholl reaction, Functional Organic Materials

Green and sustainable synthetic electrochemistry provides innovative solutions to address the challenges associated with conventional organic synthesis. To this end, one of the most prominent features of synthetic electrochemistry is its unique capability to control reactivity via "dialed-in" specific potential when necessary.[1] We herein demonstrate the unique capability of synthetic electrochemistry in the facile synthesis of diverse functional small molecules, including nitrogen-sulfurs of various oxidation states[2-4] and functional organic materials. Therefore, previously challenging transformations with conventional chemical oxidations are now readily accessible.[5]



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Electroorganic Synthesis with a Catalytic Amount of Electrical Input

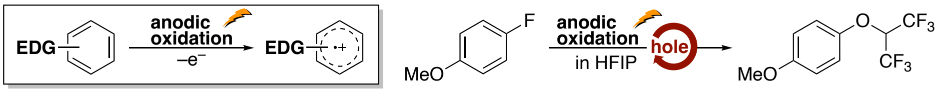
([1]*Graduate School of Environmental, Life, Natural Science and Technology, Okayama University*) ○Eisuke Sato[1]

Keywords: Organic Synthesis, Electroorganic Synthesis, Flow Synthesis, Catalyst

Since electroorganic synthesis has been attracted as a powerful tool in organic synthesis to achieve a “green” transformation, many unique chemical transformations have been reported over the past decades.[1] The irreversible electron transfer between electrodes and molecules allows oxidative or reductive transformation without any redox reagents. In contrast, we focused on the catalytic usage of electricity to construct the electron- or hole-catalyzed reaction cycles.[2] Several noteworthy reactions that proceeded with a catalytic amount of electrical input were reported,[3,4] and we also investigated electrochemical transformations with higher current efficiency.

Herein, we report recent examples of electrochemical transformation of electron-rich aromatic compounds with catalytic anodic oxidation. The anodic oxidation of the aryl fluoride, bearing methoxy group, generated the corresponding radical cation, and the following nucleophilic substitution afforded the S_NAr product.[5] When the anodic oxidation was carried in a solution of 1,1,3,3-hexafluoroisopropyl alcohol (HFIP), the HFIP adduct was obtained with a good yield with a catalytic amount of electrical input. The cyclic voltammetry and the density functional theory calculations revealed that the reaction would proceed with a hole-catalyzed pathway.

When anodic oxidation is performed, electrogenerated acid (EGA) is generated on the anodic surface, and it is known that EGA can also catalyze chemical transformations. Our preliminary investigation found that the anodic oxidation promotes Claisen rearrangement of allyl aryl ether to produce 2-allyl phenol. Although we expected the rearrangement to proceed with a hole-catalyzed mechanism, careful examination suggested that highly active borane species generated by the anodic oxidation could act as a Lewis acid to achieve Claisen rearrangement.[6]



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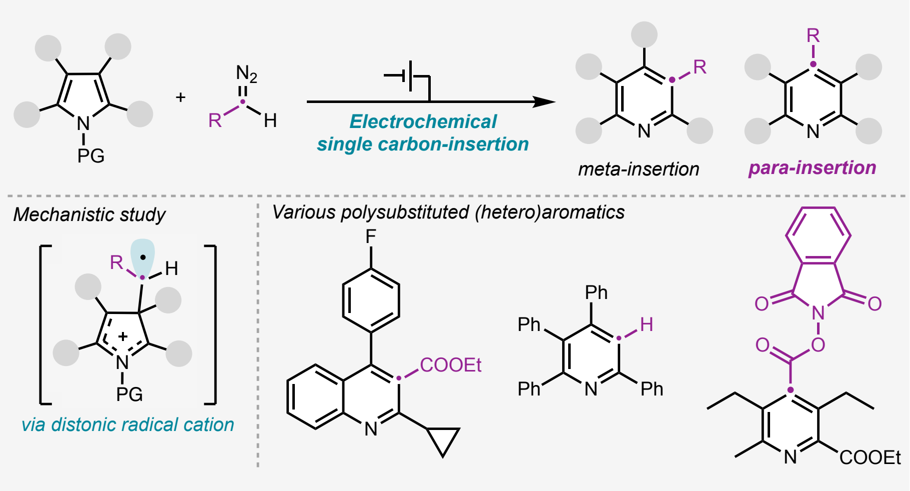
Electrochemical single-carbon insertion via distonic radical cation intermediate

([1]*Department of Chemistry and Life Science, Yokohama National University,* [2]*JST PRESTO*)
○Naoki Shida[1]

Keywords: Electrosynthesis; Insertion reaction; Skeletal editing; Distonic radical cation; Anodic oxidation

Polysubstituted (hetero)aromatic compounds are fundamental to pharmaceuticals and advanced materials, but achieving precise regioselectivity in single-carbon insertion has remained a significant challenge. This study introduces a novel electrochemical approach that enables selective single-carbon insertion into pyrrole derivatives and related substrates through anodic oxidation. The process generates reactive radical cation intermediates, which react with diazo compounds to yield selectively expanded products.

A major achievement of this work is the control over *para*-selectivity by fine-tuning the electronic properties of *N*-protecting groups. Screening experiments demonstrated that electron-withdrawing protecting groups significantly favor para-insertion, allowing access to previously challenging products. This method is applicable to a broad range of substrates, including indole, imidazole, and cyclopentadiene derivatives, resulting in diverse functionalized compounds. Mechanistic studies, supported by cyclic voltammetry (CV), in situ electron paramagnetic resonance (EPR), and density functional theory (DFT) calculations, confirmed that distonic radical cation intermediates are key to reducing the energy barrier for carbon migration and ensuring high selectivity. Moreover, flow electrolysis was utilized to enhance productivity, enabling the scalable synthesis of pharmaceutically relevant intermediates.



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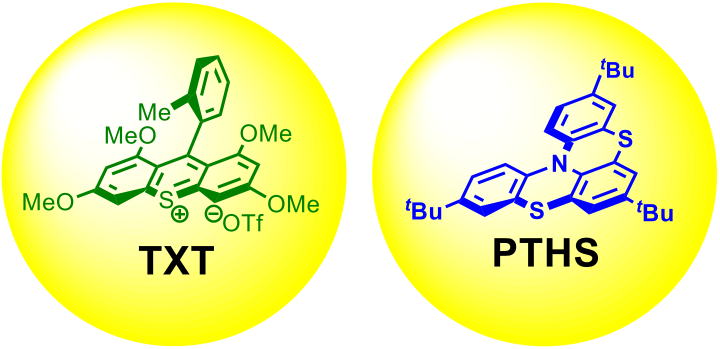
Moderately Oxidizing Thioxanthylium Organophotoredox Catalyzed Radical Cation Cycloaddition Reactions

([1] *Research Institute for Interdisciplinary Science, Okayama University*) ○Kenta Tanaka[1]

Keywords: Photoredox catalysis; Visible light; Photocatalyst; Thioxanthylium salt; Phenothiazine

Visible-light-mediated chemical transformations have attracted much attention in recent years especially with regard to designing sustainable energy conversion systems. Classically, photochemical reactions in organic synthesis have used ultraviolet (UV) light, which can damage substrates and/or products due to its high energy and thus result in undesirably complex product mixtures. To circumvent this obstacle, catalytic photoredox reactions have been developed over the past decade. While metal complexes based on ruthenium and iridium have been widely used as photoredox catalysts in these systems, the focus of interest has shifted toward the development of metal-free photoredox catalysts, which represent a more cost-effective and sustainable approach.

Recently, we have reported the design and synthesis of the thioxanthylium organophotoredox catalysts (TXT), which have moderate excited-state reduction potentials [$E_{1/2}^{\mathrm{red}*} = +1.75\sim+1.94$ V vs SCE].[1] In this presentation, I will discuss the thioxanthylium organophotoredox catalyzed radical cation cycloaddition reactions. Additionally, we have developed a new series of phenothiazine photocatalysts (PTHS), which exhibits low excited state oxidation potentials [$E_{1/2}^{\mathrm{ox}*} = -2.34\sim-2.40$ V vs SCE].[2] I will also discuss the phenothiazine organophotoredox catalyzed phosphonation of aryl halides.



Organophotoredox Catalysts

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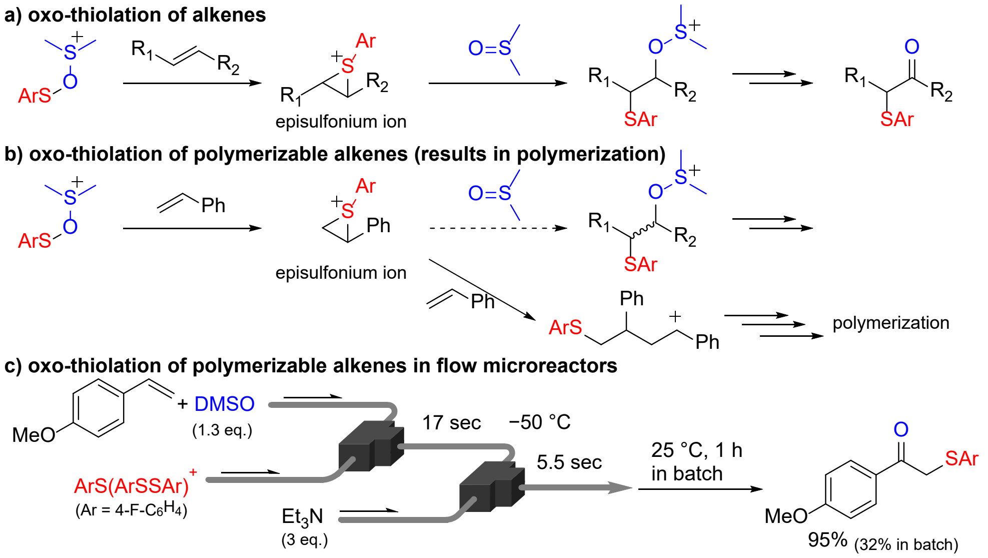
Flow Microreactor-Based Selectivity Control of Electrochemical Reactions

(*Faculty of Science, Hokkaido University*) Yosuke Ashikari

Keywords: Electrochemical Oxidation; Flow Microreactor; Selectivity Control

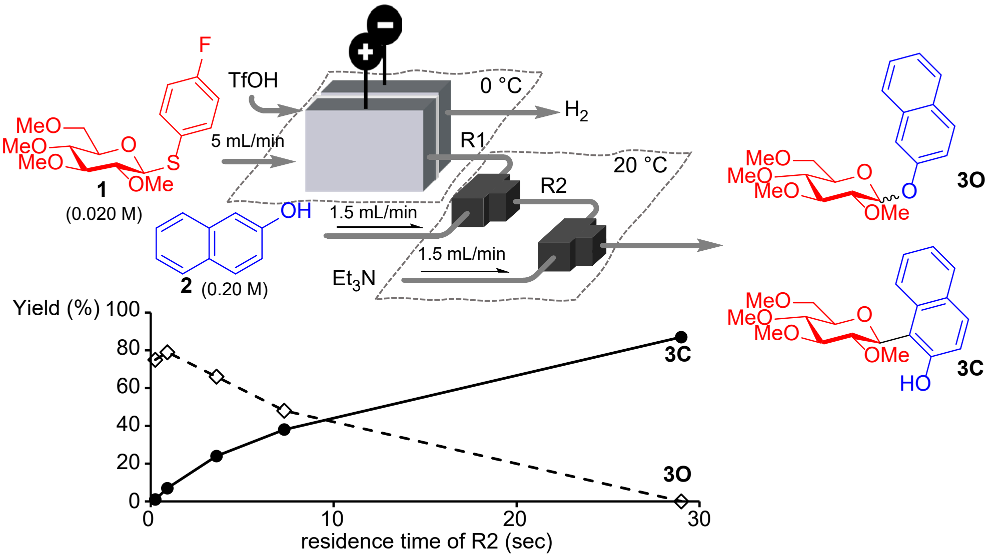
Electrochemical oxidation enables the irreversible generation of organocationic species, whose high reactivity has been utilized in various synthetic reactions. However, due to this high reactivity, reaction selectivity in electrochemical reactions can sometimes be insufficient. In this presentation, I will report the research that achieves selectivity control in electrochemical reactions by employing flow microreactors,[1] which offer excellent control over material diffusion and reaction time.

Oxo-thiolation, a kind of alkene difunctionalization reactions, can be triggered by anodically generated sulfur-cation stabilized by dimethyl sulfoxide (DMSO).[1] In this reaction, the alkenes are converted to the corresponding epi-sulfonium ions, and the three-membered ring is opened by an attack of DMSO to become an alkoxysulfonium ion (Scheme 1a). However, the oxo-thiolation of polymerizable alkenes, such as styrene, results in low yields because unreacted styrene can react with the epi-sulfonium ion to be polymerized (Scheme 1b). To increase the selectivity, we utilized (1) a more reactive sulfur-cation, and (2) the flow microreactor to convert the alkenes to the epi-sulfonium ions before they oligomerize. Using the flow microreactor shown in Scheme 1c, we achieved oxo-thiolation of polymerizable alkenes in a high yield. Especially in high temperatures, the use of the flow microreactor was critical to control the selectivity, suggesting the rapid mixing of the reagents is important in this reaction.[3]



Scheme 1. Selectivity control by rapid mixing. Ar means aryl group (typically 4-F-C_6H_4).

The time-controllability of flow microreactor also serves as a powerful method to control the selectivity. We investigated the synthesis of phenolic glycosides from reactions of anodically generated glycosyl cations with phenols. We have reported that, in a batch condition, the reaction of a glycosyl cation, which was generated from thioglycoside **1**, with 2-naphthol (**2**) provides phenolic *C*-glycoside **3C**, where the carbon atom of **2** is attached to the anomeric carbon.[4] Since it is known that phenolic *C*-glycosides are basically generated from *O*-*C* rearrangement[5] of the corresponding *O*-glycosides, we investigated selectivity control of this rearrangement by time. In the flow microreactor shown in Scheme 2, 1 was anodically oxidized and mixed with 2, followed by a quenching with triethylamine after the residence time of reactor R2 (t^{R2}). When t^{R2} was 30 seconds, **3C** was selectivity obtained. When decreasing t^{R2}, the yield of the *O*-glycoside (**3O**) increased, and finally, with 0.3 second of t^{R2}, **3O** was selectively obtained. These results indicate that the time controllability of the flow microreactor can control the generation of phenolic *O*- and *C*-glycosides even though their rearrangement finishes within 1 minute.[5]



Scheme 2. Selectivity control by time-control

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Electrochemistry Unlocks New Possibilities in Alkene Functionalization

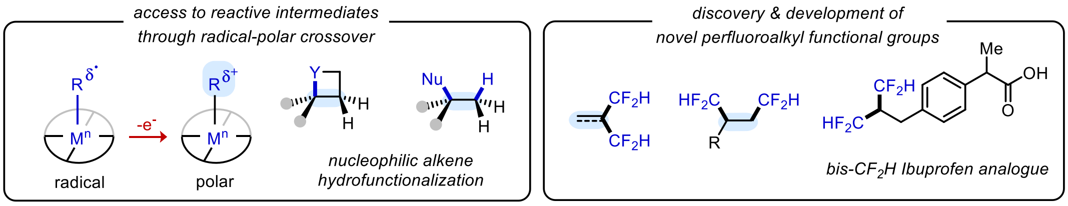
([1]*Department of Chemistry, Pohang University of Science and Technology (POSTECH)*) ○ Hyunwoo Kim[1]

Keywords: Electrocatalysis; Alkene Functionalization; Homogenous Catalysis; Bioisosteres; Radical Reactions

Alkene functionalization plays a pivotal role in expanding the repertoire of synthetic methods and enhancing the complexity of organic compounds providing an "escape from flatland". Recent advances include the development of regioselective alkene hydrofunctionalization, with metal-catalyzed hydrogen atom transfer (MHAT) emerging as a key strategy for adding structural diversity from alkene starting materials.

In the first part of the talk, the strategic application of electricity in cobalt-MHAT catalysis will be discussed, which could provide a new way for the reactive intermediate to outcompete undesired side reactions.[1] A wide range of coupling partners encompassing weak nucleophiles such as phenols could successfully engage in various electrocatalytic conditions with high chemoselectivity.[2] Moreover, this electrocatalytic platform has the potential to function as an efficient bypass for unfavorable intramolecular reactions which possess inherent kinetic challenges.[3]

In the second part, difluoromethylative functionalization of unsaturated C–C bonds under electrochemical conditions will be discussed. Despite the high prevalence and importance of vicinal hydrogen bond donors in pharmaceutical agents, a general synthetic method for doubly difluoromethylated compounds remains extremely rare. By leveraging electrochemistry to oxidize $Zn(CF_2H)_2(DMPU)_2$–a conventionally utilized anionic transmetalating source–we paved a way to utilize it as both CF_2H radical and anion source to deliver CF_2H groups in both terminal and internal position of alkenes, thereby granting access to doubly-difluoromethylated alkanes which hold significant potential in medicinal chemistry.[4,5]



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