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# Keynote Lecture: Aromatic Metamorphosis

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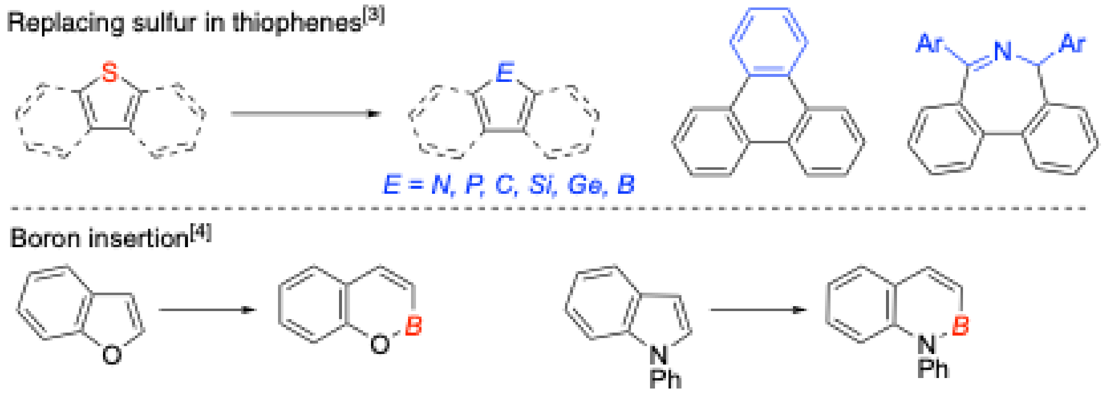
## Abstract

Aromatic skeletons are generally resistant to cleavage due to their high stabilization energy and strong endocyclic bonds. While exocyclic functionalizations are well explored, endocyclic modifications via partial disassembly and ring reconstruction remain less studied. Here, I disclose our efforts to establish 'aromatic metamorphosis',[1] a strategy that transforms common aromatic compounds such as thiophenes, benzofurans, and indoles into distinct ring systems through multi-step or ideally single-step processes. Aromatic metamorphosis, or what we may now call skeletal editing[2] of an aromatic ring, challenges traditional frameworks in organic chemistry and provides new efficient or sustainable tools for synthesizing otherwise inaccessible heterocycles and generating chemical libraries with diverse endocyclic frameworks.[3,4]



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# Keynote Lecture: Light, Organocatalysis s Enzymes: New Radical Opportunities

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## Abstract

The combination of photocatalysis, biocatalysis, and organocatalysis provides a powerful yet underexplored strategy for addressing major challenges in asymmetric synthesis[1]. By combining these distinct catalytic disciplines, we aim to develop novel enantioselective radical processes that are otherwise difficult to achieve using conventional approaches. Central to this concept is the ability to harness enzyme-bound organocatalytic intermediates as photoactive intermediates, unlocking new mechanistic pathways for radical generation and control.

Recently, we developed a new approach to light-driven biocatalysis, where engineered enzymes utilize iminium ion intermediates—formed transiently within their active sites—as single-electron oxidants upon visible-light excitation[2]. This strategy enables the activation of chiral carboxylic acids, triggering radical decarboxylation and subsequent stereospecific cross-coupling to construct complex chiral architectures with multiple stereocenters and complete enantiocontrol. Notably, the enzyme's active site prevents racemization of chiral radicals via a rare "memory of chirality" mechanism, ensuring high stereochemical fidelity. By leveraging the unique synergy between light, biocatalysts, and organocatalytic intermediates, this work expands the scope of radical chemistry and sets the stage for new, sustainable methods in asymmetric synthesis.

**Keywords**: light, photochemistry, organocatalysis, biocatalysis
**Acknowledgements**: This research is supported by the European Research Council (ERC- 2023-AdG 101141690 – PHOTOZYME).

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# Control of $CO_2$ Reduction Selectivity by Simultaneous Optimization of Ag-Doped Cu Catalysts and Catalyst Layer Structures

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## Abstract

Electrochemical carbon dioxide reduction reaction ($CO_2RR$) offers a sustainable route to convert $CO_2$ into value-added products using renewable electricity. Copper (Cu) is known as the only catalyst capable of producing multi-carbon products such as ethylene ($C_2H_4$),[1] although its selectivity is limited under neutral conditions. Gas diffusion electrodes (GDEs) have attracted attention for practical $CO_2$ electrolysis since GDEs enable high-current $CO_2$ electrolysis, where mass transport of reactants and intermediates within the porous catalyst layer plays a critical role in determining the overall performance. [2] In this context, we have also found that, in gold (Au)-loaded gas diffusion electrodes (GDEs), electrode parameters such as loading strongly affect the $CO_2RR$ selectivity,[3] suggesting the general importance of electrode structural optimization. In this study, Ag-doped Cu nanoparticles (Ag/Cu), which have been reported to act as efficient $CO_2RR$ catalysts,[4] were synthesized. They were supported on GDEs, and the catalyst loading was systematically varied to investigate the effects on $CO_2RR$ selectivity.

Ag/Cu nanoparticles were prepared by refluxing Cu nanoparticles in ethanol with $AgNO_3$, and then deposited on GDEs with different loadings (10–100 μg $cm^{-2}$). $CO_2RR$ activity was evaluated in 1 M $KHCO_3$ under constant current conditions with a custom-made electrochemical cell.

The results showed that both Ag content and catalyst loading strongly influenced product selectivity. At low loading, methane ($CH_4$) was dominant, while higher loading promoted ethylene formation. With 1 mol% Ag doping, the ethylene selectivity reached 44% at 300 mA $cm^{-2}$, higher than undoped Cu (Figure 1). These findings demonstrate that catalyst layer engineering, combined with controlled Ag incorporation, can effectively shift $CO_2RR$ selectivity toward C2 pathways.[5]

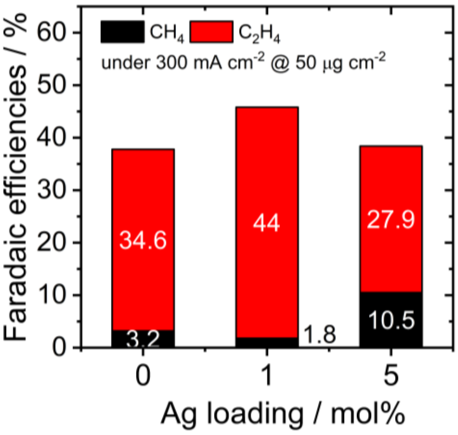

*Figure 1 Faradaic efficiencies of $C_2H_4$ and $CH_4$ for Cu catalysts with different Ag loadings. The measurements were conducted at a current density of 300 mA $cm^{-2}$ with a catalyst loading of 50 μg $cm^{-2}$.*

**Keywords**: $CO_2$ reduction, gas diffusion electrode, Cu catalyst, product selectivity

**Acknowledgements**: This research is partially supported by JST PRESTO program (JPMJPR2371).

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# New Strategies in Bicyclo[1.1.0]butanes Chemistry: Au-Catalysis and Electrosynthesis

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## Abstract

Bicyclo[1.1.0]butanes (BCBs) **1** have recently gained significant attention due to their highly strained, non-planar structure composed of two fused cyclopropane rings. This unique geometry imparts a distinct three-dimensional shape and electronic profile, positioning BCBs as valuable starting materials to prepare $C(sp^3)$-rich bio-isosteres for replacing planar aromatic rings in drug design.[1]

Following our interest for the development of novel Au-catalyzed reactions,[2] we are disclosing a new dual-activation strategy for the regio- and chemoselective functionalization of BCBs, where the role of gold is to both activate **1** and to generate the electrophilic reaction partner from electron-rich allenes **2**.[3] A catalyst- and substrate-controlled chemodivergent process can be realized to direct the reactivity either to chiral (enantioenriched) cyclobutene derivatives **3** or to biologically relevant bicyclo[2.1.1.]hexanes **4.**

Furthermore, given our recent interest in electrochemical organic synthesis,[4] we are subjecting BCB-derivatives to unprecedented oxidative cyclization processes, toward highly decorated oxa-bicyclo[3.1.1]heptanes **5**.

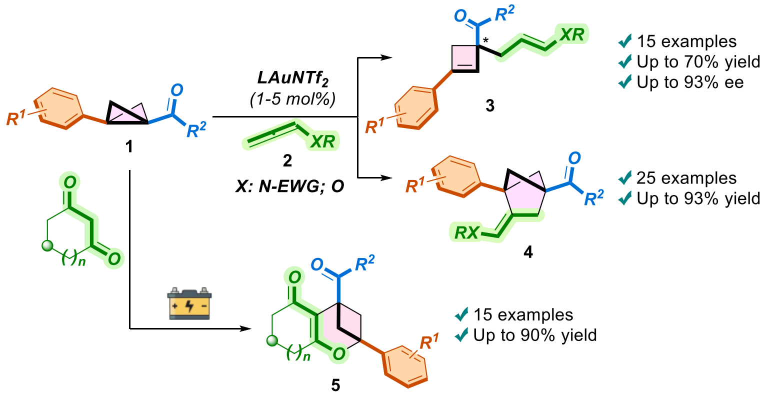

*Figure 1: Gold Catalysis and Electrosynthesis in BCB functionalization*

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# Rational Design of the Electric Double Layer for Gaseous $CO_2$ Reduction to Multicarbon Products

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## Abstract

$CO_2$ electrolysis for the production of value-added products is a promising technology for closing the carbon cycle and converting anthropogenic $CO_2$ into chemical feedstocks [1-4]. For practical $CO_2$RR applications, it is essential to improve energy efficiency, selectivity toward high-value products, and production rates. In particular, achieving high current density and energy-efficient formation of multicarbon ($C_{2+}$) products, such as ethylene, ethanol, acetic acid, and n-propanol, is crucial.

Recently, we achieved a record partial current density of 1.7 A $cm^{-2}$ for $CO_2$ electroreduction to $C_{2+}$ products using gas diffusion electrodes (GDEs) loaded with Cu nanoparticles [5-7]. However, this system employed liquid electrolytes as the catholyte, leading to significant ohmic losses that reduced energy efficiency, particularly under high-current operating conditions. To address this limitation, researchers have increasingly adopted membrane electrode assembly (MEA) electrolyzers with anion exchange membrane electrolytes for $CO_2$ electrolysis.

Herein, we investigate the operating principles of MEAs for $CO_2$ reduction to $C_{2+}$ products, with a particular focus on the structure of the electric double layer (EDL) at the cathode surface. As a result, we found that alkali metal cations crossing over from the anolyte to the cathode surface were involved in the formation of the EDL during $C_{2+}$ generation in the MEAs [8].

Furthermore, we conducted $CO_2$RR in aqueous solutions containing tetraalkylammonium cations to investigate the effect of cation species on product formation. We confirmed that ethylene production rates increased when smaller cations were used. Numerical simulations show that smaller cations intensify the electric fields within the EDL, boosting $C_{2+}$ formation [9]. These findings offer valuable insights into the design of MEA electrolysis systems fed with pure water.

**Acknowledgements**: This work was supported by JST-CREST (JPMJCR24S6 and JPMJCR18R3), and Moonshot Research Program (Grant 20001627-0).

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# Expanding the Toolbox of Visible Light-Activated Photoredox Catalysis

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## Abstract

The latest progress in photoredox catalysis has focused on a wide range of chemical reactions, in which an organic or inorganic chromophore initiates a cascade of electron-transfer events, often in conjunction with a transition metal catalyst [1].

While several classes of chromophores with tailored photophysical and electrochemical properties at the excited state have been employed as suitable photocatalysts [2,3], the need to trigger the reactivity of highly energy-demanding compounds prompts the quest for powerful reductants. More recently, with the aim to target challenging substrates, we broadened the landscape of the active species in visible light-activated reactions, identifying strong photoreductants in luminescent Meisenheimer complexes [4]. In addition, we have investigated the role of solvated electrons [5,6] as the main reducing species in photoredox-activated processes.

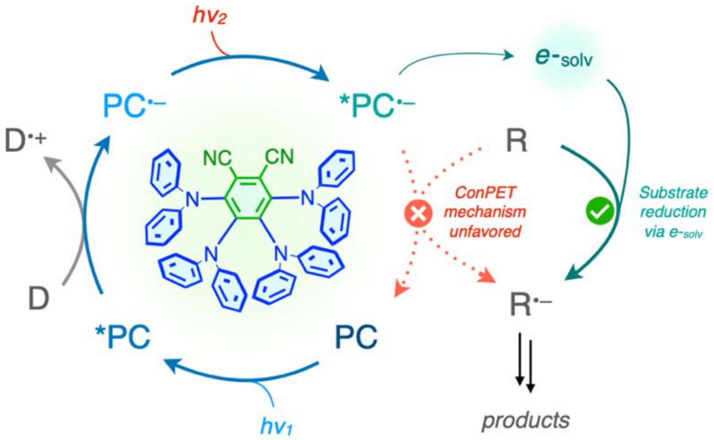

*Figure 2: Reduction of organic substrates via formation of solvated electrons*

**Keywords**: excited states, metallaphotoredox catalysis, thermally activated delayed fluorescence, solvated electron

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# Electrochemical imaging by scanning electrochemical cell microscopy

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For the global pursuit of a carbon-neutral society, electrochemical energy devices have been paid great attentions. The performance of these devices is critically dependent on the optimization of material composition and structural design, particularly through precise control at the nano-/atomic-scale structures in low dimensionality. A challenge remains in the comprehensive analysis of the microscopic electrochemical properties of these advanced materials. To address it, a variety of analytical techniques are employed, including electron microscopy, synchrotron radiation analysis, and scanning probe microscopy (SPM), each selected and adapted to fulfill specific measurement demands. Among these, SPM is advantageous for conducting in-situ measurements during electrochemical reactions. Scanning electrochemical microscopy (SECM) has attracted considerable interest due to its capability for high spatial resolution imaging. Since its initial development by A. J. Bard in 1989[1], numerous SECM and related systems have emerged[2]. Of particular interest is scanning electrochemical cell microscopy (SECCM), which utilizes a pipette filled with electrolyte solution and equipped with a quasi-reference/counter electrode (QRCE) to form a localized droplet on the sample surface, effectively creating a confined electrochemical cell as shown in Figure 1. This configuration enables highly localized electrochemical measurements with excellent spatial resolution and sensitivity. In this talk, we will report on the visualization of electrochemical reactions on low-dimensional materials using SECCM such as lithium-ion batteries[3], redox mediator[4] and electrocatalysts[5,6] but also the effects of chemical dopants[7], functionalization through defect engineering[8], material manipulation[9].

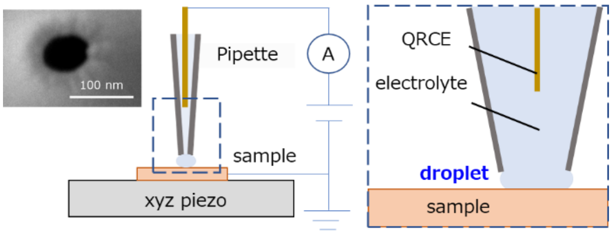

*Figure 1: A schematic of SECCM system with a 50 nm diameter glass pipette (inserted).*

**Keywords**: scanning electrochemical cell microscopy, electrocatalysts, lithium-ion battery

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# Developing Nickel Organometallic Nucleophilic Reagents via Photoredox Catalysis

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## Abstract

The addition of organometallic reagents to the carbonyl group represents a key transformation, both in Academia and industry. Most of these transformations rely on a mechanism in which accessible and reactive halides are transformed into the corresponding nucleophilic organometallic reactive compounds through a redox mechanism, using a metal (Cr, Mg, Ni, etc.) in low oxidation state, by electron transfer. Using dual photoredox catalysis, reactive nucleophilic organometallic intermediates, useful in reaction with electrophiles, can be prepared in sustainable manner, avoiding the use of metals in low oxidation state [1]. Herein we report our research program towards the rediscovery and use of nickel organo-metallic reagents, introduced by Corey, Hegedus, and Semmelack many years ago. The results unveiled the extraordinary capabilities of photoredox catalysis, enabling the creation and efficient utilization of potent nucleophilic organometallic reagents under mild conditions, free from the need for strong bases or stoichiometric metal reductants. Reformatsky-type reactions, vinylation [2] and allylation [3] of aldehydes with different substituted allyls moieties will be discussed.

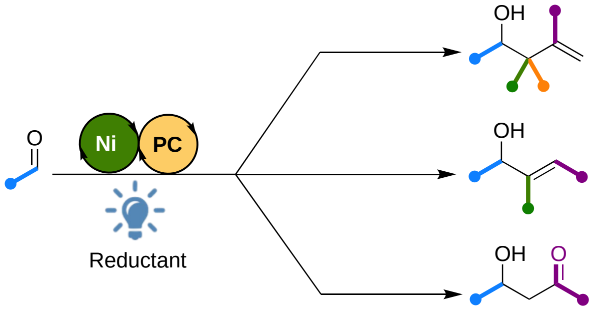

*Figure 3*

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# Photocatalytic Grignard-Barbier reaction using feedstock molecules

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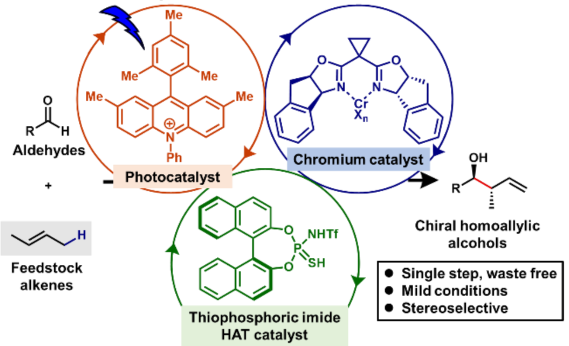
## Abstract

The nucleophilic addition of organometallic reagents such as Grignard reagents to carbonyl compounds constitutes a fundamental transformation for the synthesis of alcohols. However, conventional methodologies for alcohol synthesis typically involve multi-step procedures, generating substantial waste and exhibiting limited functional group tolerance. The ability to directly generate nucleophilic organometallic species from readily available hydrocarbons would enable the step and atom economical synthesis of fine chemicals from petroleum-based resources. To address these issues, I have developed an original methodology that employs multiple catalysts as an integrated system. This catalytic system comprises three key components: a hydrogen atom transfer (HAT) catalyst to cleave C–H bonds, a metal catalyst to promote the desired transformation, and a photocatalyst that electronically couples the two other catalysts.

As a proof of concept, I focused on the development of a catalytic enantioselective allylation of aldehydes using simple hydrocarbon alkenes. By introducing a thiophosphoric imide as a uniquely effective HAT catalyst into a system comprising a chiral chromium complex and an acridinium-based photocatalyst, the enantioselective addition of alkenes to aldehydes was successfully realized via allylchromium intermediates (Figure 1).[1] This transformation proceeded with high reactivity and excellent selectivity, even in the presence of various functional groups. Building on this platform, I have expanded the methodology to encompass diverse selectivity controls, broadened substrate scope, and applications in the synthesis of synthetically and biologically important molecules.[2]



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Related works: *Org. Lett.* **2020**, *22*, 8584.; *Org. Lett.* **2022**, *24*, 1486.; *Adv. Synth. Catal.* **2022**, *364*, 3378.; *J. Org. Chem.* **2023**, *88*, 6333.; *Angew. Chem. Int. Ed.* **2025**, *64*, e202503249.

*Figure 4: Application to nucleophilic addition reaction using ternary catalyst system*

**Keywords**: photoredox catalyst, HAT catalyst, chromium catalyst, C-H activation
**Acknowledgements**: We thank Prof. Kanai and lab members (The University of Tokyo) for fruitful discussion and support. This research was supported by JSPS KAKENHI grant numbers JP20H05843 (Dynamic Exciton) and JP21K15220, and JST-PRESTO Grant Numbers JPMJPR2279.

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# New synthetic protocols to unlock greenness in peptide synthesis: from unprotected to hybrid chemoenzymatic approaches

**L. Ferrazzano[1], D. Corbisiero[1], T. Fantoni[1], S. Rizzo[1], I. Di Stefano[1], N. Patrian[1], A. Tolomelli[1], and W. Cabri[1]**

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## Abstract

The development of greener synthesis processes is essential to transforming the industrial landscape— particularly in the pharmaceutical sector—into a sustainable, long-term reality. The resurgence of peptides as medical treatments, coupled with stricter sustainability demands from regulatory agencies, has driven chemists to introduce environmentally friendly methods for producing highly pure active pharmaceutical ingredients (APIs). Over the past five years, we have contributed to advancing innovative, sustainable methodologies for solid-phase peptide synthesis (SPPS)[1-4], liquid-phase peptide synthesis (LPPS)[5], and chemoenzymatic peptide synthesis (CEPS)[6]. In this context, one of our recent key focuses has been the removal of side-chain orthogonal protective groups from arginine and histidine to enhance the sustainability of SPPS by increasing peptide atom economy (AE) and reducing impurities during final cleavage. By optimizing the combination of OxymaPure and tert-butyl ethyl carbodiimide (TBEC) in green solvents, we successfully synthesized intermediates of etelcalcetide and vasopressin, as well as key fragments of liraglutide, via SPPS.[4] Furthermore, the OxymaPure/TBEC protocol in NBP/DMC was applied to sequences containing unprotected side-chain arginine, histidine, tryptophan, and tyrosine. Simultaneously, by leveraging green solvent mixtures for the synthesis of liraglutide fragments, we developed a hybrid chemoenzymatic approach (CEPS) that utilizes a ligase enzyme's selectivity for fragment coupling.[6] This approach, applied to liraglutide synthesis, improved waste quality in upstream processes, reduced solvent volumes during downstream purification, and resulted in higher purity of the target peptide.

**Keywords**: peptide, chemoenzymatic approaches, solid-phase peptide synthesis, liquid-phase peptide synthesis

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# Direct Amidation of Unactivated Esters Using Cage-Shaped Aluminum Complexes

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## Abstract

Amides are indispensable structural motifs in natural products, pharmaceuticals, and functional materials, and a wide range of synthetic methods for their preparation have been developed. Among them, direct amidation of esters represents an atom-economical and operationally simple approach. Nevertheless, its broader application has been hampered by the requirement for harsh reaction conditions, limited substrate scope, and poor functional group tolerance. In our previous work, we demonstrated that a cage-shaped aluminum complex could catalyze highly stereoselective glycosylation reactions,[1] in which an imidate was activated through a unique highly coordinated state. Building on this concept, we have now discovered that the same cage-shaped aluminum complex effectively activates esters toward nucleophilic attack by amines, enabling direct amide bond formation under mild conditions (Figure 1). Notably, this catalytic system exhibited broad applicability to a variety of esters, including unreactive triacylglycerols, which are generally inert toward conventional Lewis acid catalysts. The present study thus expands the scope of aluminum-based catalysis and offers a new strategy for efficient amide synthesis from abundant and stable ester feedstocks.

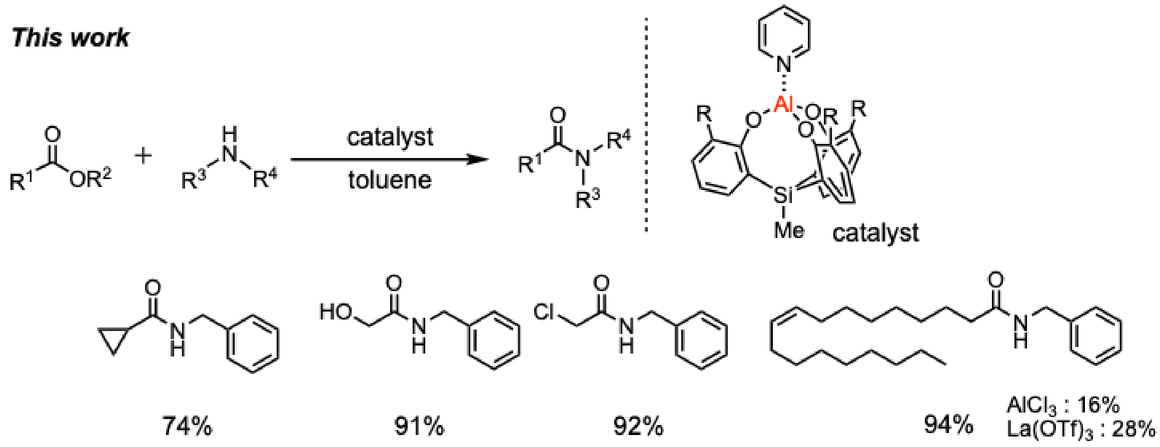

*Figure 5: Direct Amidation of Esters*

**Keywords**: amides, aluminum, direct amidation

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# Chemical Synthesis and Immune Functions of Bacterial Lipid A for Safe Vaccine Adjuvant Development

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## Abstract

Lipopolysaccharide (LPS) is a major glycoconjugate in the outer membrane of Gram-negative bacteria and canonical *Escherichia coli* LPS activates innate immunity to induce lethal strong inflammation. The terminal glycolipid lipid A is the active principle of LPS. We have anticipated that low-inflammatory lipid A molecules could serve as promising vaccine adjuvant candidates.

We hypothesized that co-evolved parasitic and symbiotic bacterial components modulate host immunity in a moderate manner with low toxicity. To test this, we synthesized lipid A molecules from both parasitic and symbiotic bacteria, elucidated the molecular basis of immunoregulation, and developed safe and effective adjuvants. In this presentation, we focus on the chemical synthesis and functional analysis of lipid A from *Alcaligenes faecalis*, a bacterium inhabiting gut-associated lymphoid tissue (GALT), responsible for mucosal immune regulation. We synthesized *A. faecalis* lipid A **1**-**3** (Figure 1) with diverse acyl group patterns and identified the active center as the hexa-acylated compound **3** [2]. Lipid A **3** was confirmed to be non-toxic while retaining potent adjuvant activity.

*Acetobacter pasteurianus* is a Gram-negative bacterium used in the fermentation process of traditional Japanese black rice vinegar (kurozu). *A. pasteurianus* LPS, which is a candidate of immunostimulatory component of kurozu, contains lipid A with a distinctive structure. Here, we considered *A. pasteurianus* lipid A as a pool of acid resistant immunostimulants whose safety is ensured by food experience. We achieved the systematic synthesis of three *A. pasteurianus* lipid A molecules and identified lipid A **4** as the active center (Figure 1) [3]. Glucuronic acid residue of lipid A was found to be important for both immune function and acid resistance.

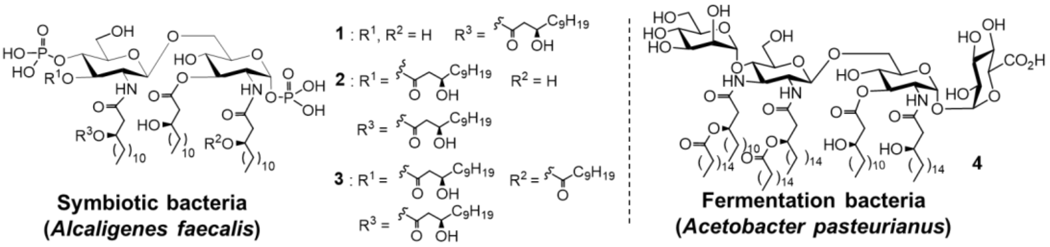

*Figure 6: Chemical structures of synthesized lipid As*

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# Green Mechanochemical Synthesis of a Photochromic Compound for Cold Chain Monitoring

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**Abstract**

In this work, I will present a sustainable, green mechanochemical approach [1] for the synthesis of a family of N-salicylideneaniline derivatives (anils) [2], designed to act as colorimetric indicators for temperature excursions. Among the synthesized compounds, a tetrafluorinated derivative exhibited robust photochromic behavior, with a distinct and persistent color change from white to red upon UV irradiation, and slow fading at low temperatures.

The selected compound was embedded into a biocompatible carboxymethyl cellulose (CMC) matrix to produce a flexible, transparent composite film. The resulting material retained its photochromic properties, showing excellent stability and responsiveness across a range of temperatures. Notably, the red coloration persisted for over seven weeks at −19 °C and 4 °C, while fading rapidly at room temperature, making it ideal for visual cold chain tracking (Figure 1).

This study demonstrates the potential of solvent-free mechanochemistry as a green synthetic route for functional materials, and highlights the applicability of cellulose-based photochromic films as low-cost, reusable, and scalable sensors for cold chain logistics [3].

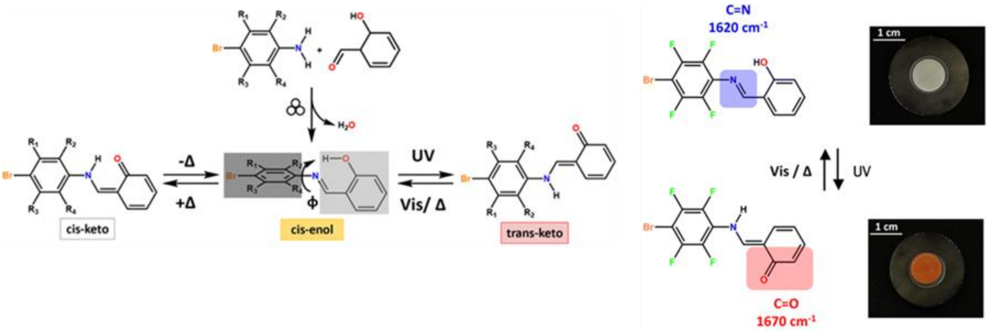

*Figure 7: Mechanochemical synthesis and reversible photochromic transformation within the CMC matrix.*

**Keywords**: Photochromic Compounds, Cellulose-Based Polymers, Cold-Chain

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# Versatile Method for the Synthesis of Aminobenziodoxolones Using Amines and Its Application to Oxidative Amination of Arylboronic Acids

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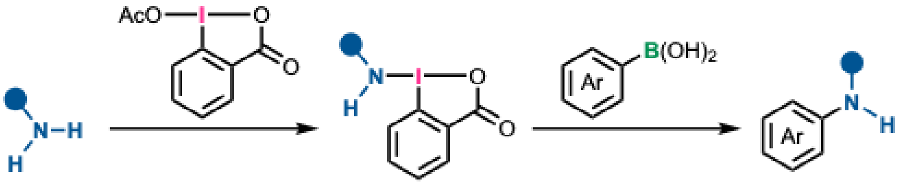
## Abstract

Hypervalent iodine(III) compounds bearing transferable nitrogen functional groups—commonly known as amino-$\lambda^3$-iodanes—have long been recognized as useful reagents for oxidative amination, a valuable strategy for constructing nitrogen-containing molecules.[1] However, their broader application has been limited by the scarce availability of suitable reagents, particularly those derived from aliphatic and aromatic amines. We herein report a versatile and practical method for synthesizing amino-$\lambda^3$-iodanes and demonstrate their use in the transition-metal-free oxidative amination of arylboronic acids. A straightforward protocol was established for the preparation of aminobenziodoxolones from readily available amines, including ammonia, primary amines, and secondary amines. This approach significantly broadens the scope of accessible amino-$\lambda^3$-iodanes beyond what has previously been reported. The resulting aminobenziodoxolones were effectively employed in the oxidative amination of arylboronic acids, enabling the efficient synthesis of a variety of arylamines. Furthermore, the in situ generation of aminobenziodoxolones from amines allows for a convenient one-pot coupling protocol with arylboronic acids, providing a transition-metal-free alternative to the classical Chan–Lam–Evans coupling.



**Keywords**: amination, hypervalent iodine, synthetic methods

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# Optical resolution of H/D isotopic chiral molecule

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## Abstract

Hydrogen- and deuterium-substitution-based chirality—H/D isotopic chiral compounds—remains unresolvable into optically pure forms from their enantimeric mixtures using current methods such as diastereomeric salt formation and chiral HPLC, because there is no significant stereochemical difference between the isotopes.

Therefore, we reasoned that exploiting the difference in bond dissociation energy between isotopes—although small, it is the largest among their distinctions—could create a rate difference between the isotopic enantiomers, thereby enabling the kinetic resolution of isotopic chirality.

Based on this hypothesis, we successfully resolved a racemic mixture of such molecules into an optically nearly pure form by employing Ru-catalyzed asymmetric C–H amination.[1]

Under the conditions of asymmetric amination using a ruthenium–salen complex, investigation of racemic 1-$d_1$-ethylbenzene derivatives revealed that the reaction proceeded with a maximum selectivity factor (S) of 83.1, allowing the isolation of nearly enantiomerically pure 1-$d_1$-ethylbenzene compounds.

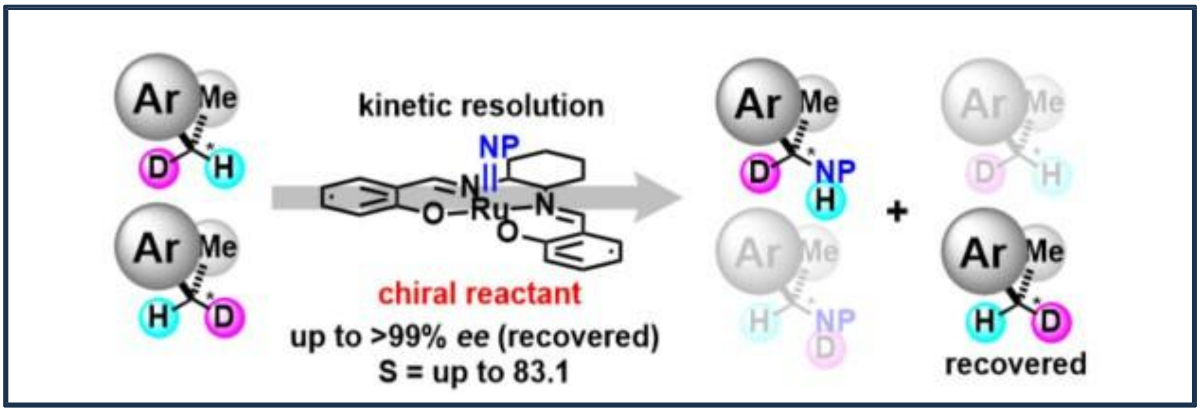

*Figure 1: Kinetic resolution of H/D isotopic chirality via asymmetric C-H amination.*

**Keywords**: Kinetic resolution, asymmetric C-H functionalization, isotopic chirality

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# Organocatalytic Asymmetric Electrophilic Amination of Allylic Boronates

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## Abstract

The asymmetric addition of allylic boronates to electrophiles is a powerful method for preparing chiral molecules bearing synthetically valuable allylic moieties. While effective catalytic methods exist, they have so far been limited to the enantioselective allyl- and crotyl-boration of carbonyl compounds and imines, thereby forming C-C bonds.[1-3] Here, we present a strategy that expands the scope of this catalytic asymmetric platform to include the stereoselective formation of C-N bonds.[4] We have identified an inexpensive and readily available chiral diol that catalyzes the addition of allylic boronates to azodicarboxylates, affording chiral allylic hydrazides with high stereocontrol (Fig. 1). This electrophilic amination chemistry shows a broad substrate scope and requires mild conditions, proceeding at ambient temperature. Mechanistic studies reveal that the chiral diol catalyst facilitates the formation of a chiral allylic boronate through the reversible exchange of the boron's achiral alkoxy ligand. By coordinating with the electrophilic azodicarboxylate, the substrates mutually activate each other, allowing for the stereoselective transfer of the allyl group.

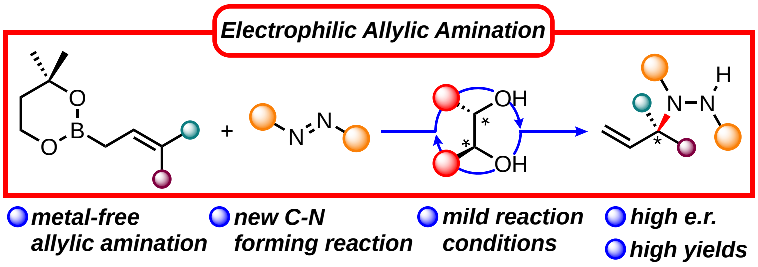

*Figure 8: Electrophilic allylic amination catalyzed by chiral diol*

**Keywords**: Electrophilic amination, chiral diol, allylic boronates, chiral hydrazides

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# Multiple NIR Chromisms of Donor–Acceptor Zwitterionic Dyes

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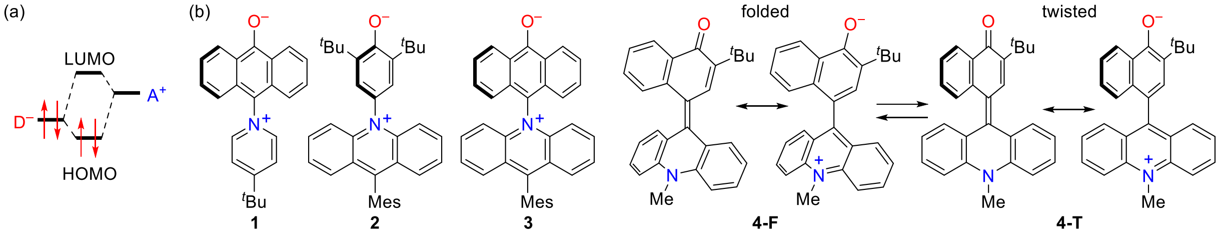
## Abstract

Organic molecules that absorb near-infrared (NIR) light have attracted attention, and switching their NIR absorption by stimuli is essential for developing highly functional organic materials.[1] While some organic molecules exhibit NIR chromisms in response to stimuli, organic molecules showing multiple NIR chromisms remain rare, limiting their utility as functional NIR dyes.

To design donor–acceptor zwitterionic dyes with NIR absorption, we combined donors with high HOMO energy levels and acceptors with low LUMO energy levels, while maintaining weak donor–acceptor interaction (Figure 1a), affording zwitterions **1–3**[2] and an overcrowded ethylene **4**.[3] **1** and **3** were synthesized utilizing the electrochemical C–N$^+$ bond formation reaction.[4] Zwitterions **1–3**, having small HOMO–LUMO energy gaps, exhibited long-wavelength absorptions in $CH_2Cl_2$ (**1**: 680 nm, **2**: 1020 nm, **3**: 1280 nm). The zwitterions **2** and **3** exhibited NIR solvatochromism, halochromism, and thermochromism. The overcrowded ethylene **4** existed in equilibrium between a folded conformer **4-F** with a smaller permanent dipole moment and visible light absorption (450 nm), and a twisted conformer **4-T** with a larger permanent dipole moment and NIR light absorption (800 nm). **4** showed multiple NIR chromisms, such as solvatochromism, thermochromism, mechanochromism, vapochromism, halochromism, and amphoteric electrochromisms, accompanying the conformational change between folded and twisted forms.



**1** $\lambda_{abs}$: 680 nm
**2** $\lambda_{abs}$: 1020 nm
**3** $\lambda_{abs}$: 1280 nm
**4-F** $\lambda_{abs}$: 450 nm
**4-T** $\lambda_{abs}$: 800 nm

*Figure 9: (a) Interaction of donor's HOMO and acceptor's LUMO, (b) zwitterions showing multiple NIR chromisms.*

**Keywords**: Zwitterions, NIR Absorption, Chromisms

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# Catalytic Hydrodefluorination of Perfluoroalkyl Substances

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## Abstract

Hydrodefluorination reactions of longer perfluoroalkyl chains remain rare. Herein, we report exhaustive hydrodefluorination reactions of pentafluoroethyl arenes and longer-chain analogues using molecular nickel catalysis.

Perfluoroalkyl substances are notorious environmental pollutants.[1] One of the notable properties of perfluoroalkyl substances is chemical and thermal stability derived from strong C(sp$^3$)−F bonds. However, their inertness hampers destruction of these materials which is inevitable to circumvent environmental pollution. Incineration of perfluoroalkyl substances requires very high temperature and has potential to produce smaller fluorinated waste.

Hydrodefluorination reaction is a possible solution to decompose perfluoroalkyl substances under mild conditions.[2] Chemists succeeded to develop a variety of hydrodefluorination reactions of a $CF_3$ group, the simplest perfluoroalkyl group. The application of hydrodefluorination for longer perfluoroalkyl, however, is limited to a single example using a carborane catalyst.[3] Herein, we disclose a nickel-catalyzed exhaustive hydrodefluorination reaction of a perfluoroethylarene using a hydrosilane.[4]

In the presence of a catalytic amount of $Ni(cod)_2$ and ICy as a ligand, and 10 equiv. (2 equiv./F) of dimethylphenylsilane, hydrodefluorination of 1-(pentafluoroethyl)naphthalene (**1**) proceeded to give 1-ethylnaphthalene (**2**) in 86% yield. Mechanistic study indicated that nickel plays multiple roles to enable this hydrodefluorination reaction.

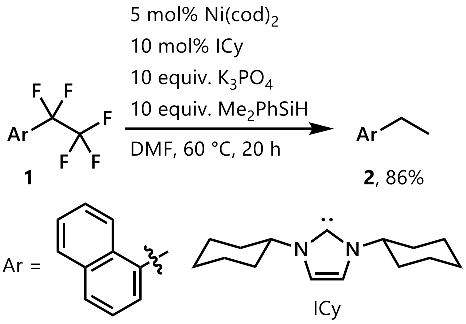

*Figure 10: Hydrodefluorination of pentafluoroethyl naphthalene*

**Keywords**: Defluorination, Nickel Catalyst, Hydrogen

**Acknowledgements**: This work was financially supported by the TOBE MAKI Scholarship Foundation, Mitsubishi Foundation, and JST PRESTO, Japan, Grant Number JPMJPR2375.

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# One-Step Esterification of Phosphoric, Phosphonic and Phosphinic Acids with Organosilicates: Phosphorus Chemical Recycling of Sewage Waste

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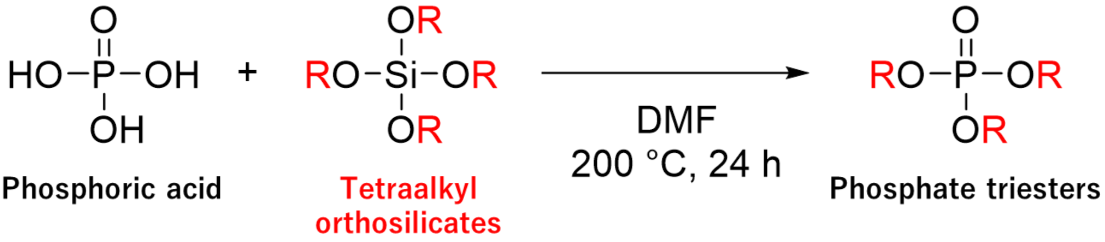
## Abstract

Global concerns about the depletion and strategic importance of phosphorus resources have increased demand for recovery and recycling. However, waste-derived phosphorus compounds, primarily as chemically inert $H_3PO_4$ or its salts, present challenges to direct conversion into high-value chemicals. Our research group developed a novel technology bypassing white phosphorus, enabling direct esterification of $H_3PO_4$ to produce phosphate triesters.[1] Tetraalkyl orthosilicates proved highly effective for the triple esterification of 85% $H_3PO_4$ and the esterification of organophosphinic and phosphonic acids. Additionally, we achieved the direct esterification of recovered $H_3PO_4$, thus pioneering a groundbreaking upcycling pathway from sewage waste to valuable phosphorus chemicals. Experimental and theoretical investigations revealed a novel mechanism, wherein tetraalkyl orthosilicates facilitate multimolecular aggregation to achieve alkyl transfer from tetraalkylorthosilicate to $H_3PO_4$ via multiple proton shuttling.



- ✓ Synthesis of phosphate esters without white phosphorus
- ✓ One-step synthesis of phosphate triesters from phosphoric acid

*Figure 11: One-step esterification of phosphoric acid with tetraalkyl orthosilicates*

**Keywords**: Phosphorus; Chemical Recycling; Silicon; Ester
**Acknowledgements**: This work was supported by JST-PRESTO (No. JPMJPR2277).

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# Generating Molecules with Artificial Intelligence

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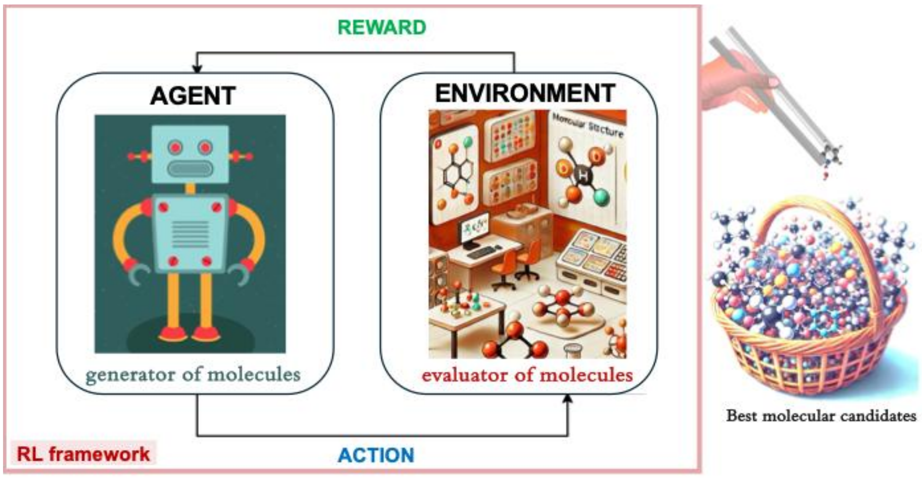
## Abstract

One of the central challenges in chemistry is the design of molecules with tailored properties, the so-called molecular inverse design (ID) problem. Addressing this challenge has profound implications across catalysis, carbon capture, energy storage, and drug discovery. [1,2] Traditional data-driven machine learning approaches have shown promise in exploring chemical spaces (CSs), but remain fundamentally limited by the need for large, high-quality datasets and costly pre-training procedures.[3,4] In this talk, I will present a novel data-free framework for molecular ID that integrates deep reinforcement learning (RL) with quantum chemistry (QC) calculations, enabling the on-the-fly generation and evaluation of molecules without any reliance on pre-existing datasets.[5] As a proof of concept, we applied this approach to toy models targeting ground- and excited-state molecular properties. Our RL-QC engine efficiently explores large CSs using first-principles chemical rewards, converging rapidly to optimal candidates and solving the ID problem within known CSs. This promising strategy represents a conceptual shift toward quantum-driven AI for molecular discovery.



**Keywords**: molecular inverse design; artificial intelligence; quantum chemistry

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# Synthesis of valuable asymmetric ketones *via* cross-ketonization

**J. De Maron[1,2], G.M. D'Onofrio[1], E. Valzano[1], T. Tabanelli[1,2], A. Fasolini[1,2], A. Allegri[1,2], S. Albonetti[1,2], F. Basile[1,2], and F. Cavani[1,2]**

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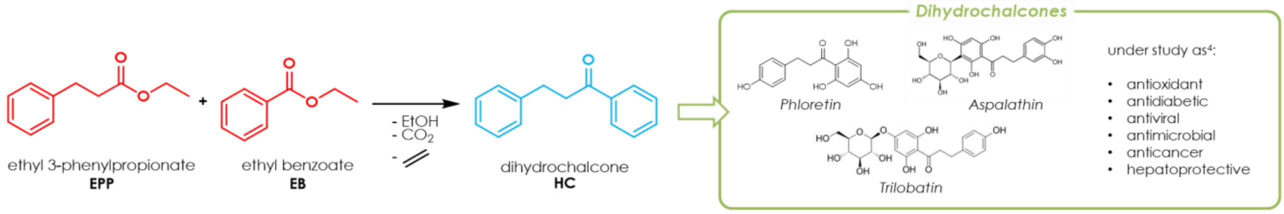
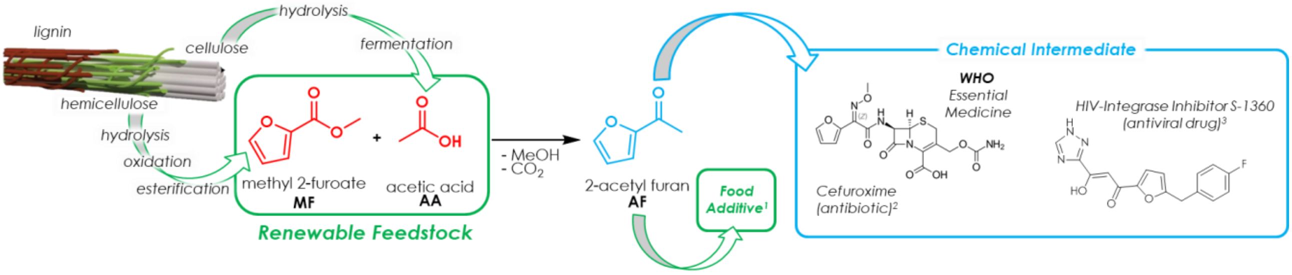
## Abstract

Valuable asymmetric ketones containing aromatic moieties are industrially produced by the Friedel-Crafts acylation of aromatics, which co-produces large amounts of unwanted regio-isomers, fails with electron-poor aromatics, and produce significant amounts of waste. Alternative methods are more selective (e.g., Heck, Suzuki, Grignard, Claysen-Schmidt, Wacker-type oxidation)[1] but often require expensive Pd-catalysts and are not economically viable on a large scale, especially to manufacture the simplest ketones. On the other hand, the selective cross-ketonization of carboxylic acids or esters in the could offer several advantages, such as continuous-flow operation and cheap heterogeneous catalysts. In this work, acetyl furan[2] (AF, food additive and intermediate in the synthesis of antibiotics and antiviral drugs) and dihydrochalcone (DHC, the simplest member of a family of compounds with interesting pharmaceutical properties) were selected as the target products, and their syntheses were investigated via the cross-ketonization between methyl 2-furoate (2-MF) and acetic acid (AA) (both obtainable from renewable resources) and between ethyl 3-phenyl propionate (E3PP) and ethyl benzoate (EB) respectively. The process was thoroughly investigated as a function of the molar ratio between reactants, temperature, and feed concentration, determining the complex reaction scheme. Then, the substrate scope was extended to several other valuable asymmetric ketones such as propionyl and butyryl furan, acetophenone, 4-methyl acetophenone, propiophenone, valerophenone, deoxybenzoin and dihydrochalcone.





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# New Molecular Transformations via Dehydrogenative Aromatization Enabled by Multifunctional Supported Metal Nanoparticle Catalysts

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## Abstract

Aromatic compounds are ubiquitously used in daily lives. The majority of synthetic methods for aromatic compounds require the use of aromatic compounds as the starting materials in multi-step manners including preliminary functionalization, such as electrophilic substitution reactions, which possess the regioselectivity limitation of *o*-, *m*-, or *p*-orientation. In this context, since Stahl et al. reported phenol synthesis from cyclohexanones using a Pd complex as the catalyst and $O_2$ as the terminal oxidant,[1] dehydrogenative aromatization has gained attention as a new method for synthesizing aromatic compounds by thermally catalyzed systems[2] as well as photoredox catalysts.[3] Since cyclohexanones can be substituted at the α-, β-, or γ-positions in regioselective manners by established classical methods, the synthesis of various substituted aromatic compounds without the limitation of *o*-, *m*-, or *p*-orientation can be enabled by dehydrogenative aromatization. However, there are still challenging dehydrogenative aromatization reactions that have not been achieved due to difficulty in controlling product selectivity and/or no effective catalysts for desired dehydrogenation.

To date, our group have developed green dehydrogenative aromatization by utilizing unique catalysis of supported metal nanoparticle catalysts, such as acceptorless primary aniline synthesis using $NH_3$ as a nitrogen source[4] and non-precious-metal-catalyzed acceptorless aromatization.[5] In this presentation, I will report our recent works on truly novel molecular transformations enabled by multifunctional supported metal nanoparticle catalysts: (i) *m*-phenylenediamine derivative synthesis catalyzed by $CeO_2$-supported Au nanoparticles[6] and (ii) azobenzene synthesis catalyzed by $Al_2O_3$-supported Au–Pd alloy nanoparticles[7] (Figure 1).

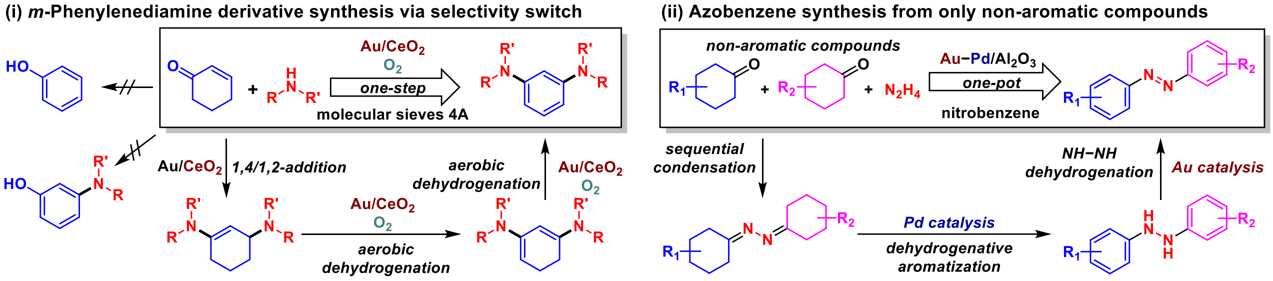

*Figure 12: Overview of this presentation*

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# Ethanol to Jet: an innovative, continuous-flow, cascade pathway to Sustainable Aviation Fuel over a multifunctional catalyst

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## Abstract

Given the ambitious targets set by the European Union to address climate change, innovative processes for producing Sustainable Aviation Fuels (SAFs) from renewable sources are being actively researched and developed. Indeed, the EU Green Deal has established a comprehensive policy framework to make energy, transport and land use systems climate-neutral by 2050, setting an interim target to reduce net greenhouse gas emissions by at least 55% by 2030. Within this framework, the “ReFuelEU Aviation” initiative plays a key role in promoting the uptake of SAFs and enabling a more sustainable air transport sector. Several SAFs alternative synthetic strategies have been investigated so far, however hydrogenated esters and fatty acids-based biofuel (HEFA) represents about 90% of all SAF produced nowadays.[1] Recently, much interest has been given to bio-ethanol (EtOH) as the starting reactant for SAFs in the so-called Ethanol to Jet (ETJ) strategy. Two different approaches are already applied at demo or commercial scale: (a) the condensation and dehydration of alcohols to mixtures of hydrocarbons and aromatic compounds over zeolites modified with a variety of cations (Vertimass approach); (b) the conversion of EtOH into a butenes-rich mixture that can be oligomerized and hydrogenated to heavier hydrocarbons for kerosene blends (Lanzajet approach). On the other hand, we’ve recently reported about an alternative process for the gas-phase, continuous-flow EtOH upgrading over a cheap, yet multifunctional, catalyst made of Cu nanoparticles supported over $ZrO_2$ based supports. Under relatively mild reaction conditions (1 atm, 300°C), this catalyst promotes a unique, cascade sequence of reactions, including alcohol dehydrogenation, Guerbet-like condensations, catalytic transfer hydrogenation and the direct dehydrogenative coupling of alcohols to esters which undergo to consecutive ketonisation finally leading to a blend of linear and branched oxygenated adducts in the C6-C14 range. This blend has similar properties, in terms of density, gross heat of combustion, flash point, freezing point and aromatics content, to those of Jet A and A-1 fuels. By precisely tailoring the properties of the non-innocent support and optimizing reaction conditions, we achieved up to 40% selectivity for the jet fuel range fraction at ethanol conversions >85%, while simultaneously enhancing catalyst stability and lifetime.[2]

**Keywords**: SAFs, ethanol upgrading, cascade process

**Acknowledgements**: GST Gestioni Servizi Tecnologie S.r.l. are acknowledged for the funding and scientific collaboration. TT and JDM also acknowledge funding from European Commission, NextGenerationEU – Piano Nazionale di Ripresa e Resilienza (PNRR) – Ministero dell’Università e della Ricerca (MUR); (project number PE_00000021).

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# Advanced sustainable organic materials: the nanocellulose promise.

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## Abstract

Nanocellulose, derived from a renewable and biodegradable material, has emerged as a key player in the field of sustainable organic materials due to its exceptional mechanical properties, high surface area, high biocompatibility and rich surface chemistry. Advances in its surface functionalization via organic reactions may open the way to a range of biomedical and advanced material applications. By tailoring its chemical interface, nanocellulose can be endowed with therapeutic functions, such as the covalent attachment of biomolecules and drugs for controlled release, or the formation of chemically crosslinked hydrogels for local treatment. At the same time, surface modifications can be designed to improve compatibility with synthetic polymers or their monomeric precursor, enabling its integration as a reinforcing component in 3D-printable systems. Together, these strategies demonstrate the versatility of nanocellulose as a sustainable and adaptable platform for next-generation functional materials.

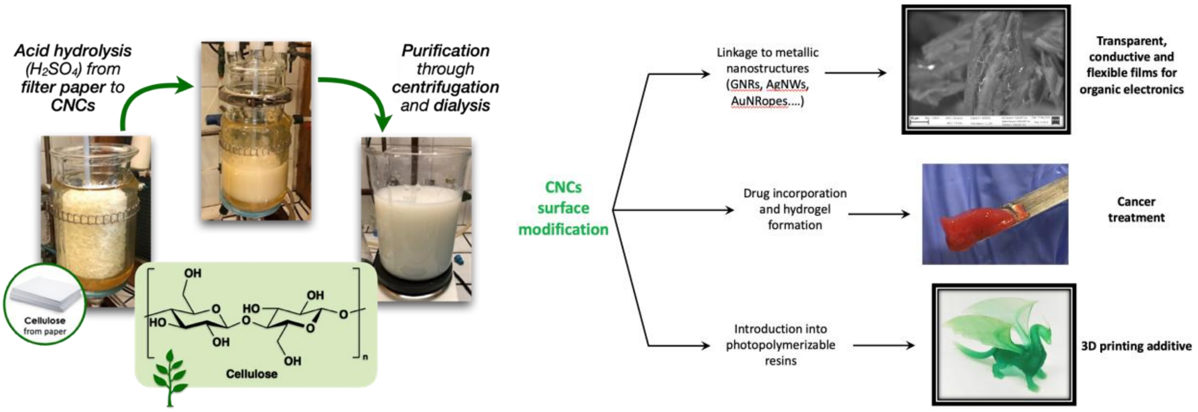

*Figure 13: Left) scale-up of nanocellulose production from filter paper. Right) Possible applications of surface modified nanocellulose.*

**Keywords**: nanocellulose, surface modification, biomaterials, drug-delivery, compatibilization.

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# Liquid-phase $CO_2$ hydrogenation in $CO_2$-dissolved expanded liquid

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## Abstract

Direct chemical conversion of $CO_2$ into valuable chemicals under mild conditions is one of the most challenging and ideal technologies for reducing $CO_2$ emissions. Multiphase reaction mixtures containing pressurized $CO_2$ and/or $H_2O$ have been investigated as an interesting reaction medium for organic synthesis. An organic liquid phase pressurized by $CO_2$ with volume expansion is referred to as a $CO_2$-dissolved expanded liquid phase (CXL)[1], and it is known that the dissolution of $CO_2$ can facilitate the dissolution of other coexisting gases, such as $H_2$, $O_2$, and CO, and promote chemical reactions involving these gases. In this study, we focused on liquid-phase $CO_2$ reduction using CXL as a new catalytic reaction medium for low-temperature $CO_2$ hydrogenation[2, 3].

First, we used different reaction media with *n*-hexane (CXL) and/or $H_2O$ for $CO_2$ hydrogenation. Table 1 shows the amount of HCOOH formed under different reaction conditions. Although *n*-hexane forms CXL phase at a $CO_2$ pressure of 5 MPa, the amount of HCOOH formed in the CXL phase was negligible (entry 1). Meanwhile, 2.39 mmol $g^{-1}$ of HCOOH was observed in the aqueous phase (entry 2). Notably, the highest amount of HCOOH (11.54 mmol $g^{-1}$) was formed in the mixed phase of CXL and $H_2O$, which was present as an emulsion in the autoclave (entry 3). This value is higher than that obtained under 1 MPa of $CO_2$ pressure without CXL formation (3.69 mmol $g^{-1}$, entry 4), suggesting that the CXL-$H_2O$ mixed reaction medium is effective for synthesizing HCOOH from $H_2$ and $CO_2$. Furthermore, the highest value obtained, 15.69 mmol $g^{-1}$, was under 2 MPa $H_2$ in the same reaction medium (entry 5), indicating that optimizing the reaction conditions would further improve the HCOOH formation rate.

*Table 1. Amount of HCOOH formed over Pd/C under various reaction conditions.*

| Entry | Gas / MPa | | Liquid phase / mL | | HCOOH / mmol $g^{-1}$ |
|---|---|---|---|---|---|
| | $H_2$ | $CO_2$ | $H_2O$ | *n*-hexane | |
| 1 | 1 | 5 | 0 | 9 | 0.08 |
| 2 | 1 | 5 | 6 | 0 | 2.39 |
| 3 | 1 | 5 | 6 | 9 | 11.54 |
| 4 | 1 | 1 | 6 | 9 | 3.69 |
| 5 | 2 | 5 | 6 | 9 | 15.69 |

**Keywords**: $CO_2$, hydrogenation, CXL, emulsion

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# Sustainable $H_2$ production from cellulose: the role of $H_2$ in the mechanism of Aqueous Phase Reforming

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## Abstract

Developing sustainable processes for H2 production from renewables is needed to push forward the H2 transition. Cellulose upgrading can involve hydrolysis of cellulose to yield glucose that can undergo the aqueous phase reforming (APR) reaction to give hydrogen. APR is a catalytic process that yields hydrogen and carbon monoxide from substrates such as glycerol or glucose at 200- 250°C [1,2]. However, glucose can easily decompose at those temperatures forming solid humins by polymerization, which block the catalytic sites and hinder hindering hydrogen generation. Here, a novel approach was used that encompass a one pot process where the hydrolysis of cellulose Is carried out together with APR, by directly employing cellulose in this process. This allowed to control the hydrolysis was carried out, producing low concentrations of glucose that were readily consumed by APR, avoiding humins formation. However, this approach requires the employment of tailored catalysts and here we demonstrate the use of layered double hydroxides (LDH) to obtain Ni-Mg-Al based catalyst active in the APR process. Using LDH precursors, Ni or PtNi over a MgAl mixed oxide were obtained and characterized by means of XRD, nitrogen physisorption, TEM, TPD and TPR analyses. In the APR test conducted in autoclave at 250°C using cellulose pulp, the use of different catalyst allowed to determine the reaction mechanism and the hydrogen production route. The addition of Pt to the Ni-based catalyst further increased the H2 yield and interestingly, providing a reducing atmosphere (1 atm of H2 at r.t.), influences the humin formation pathway, unlocking the hydrogen prodction ones, further allowing to understand that the hydrogen production pathway needs an hydrogenation step.

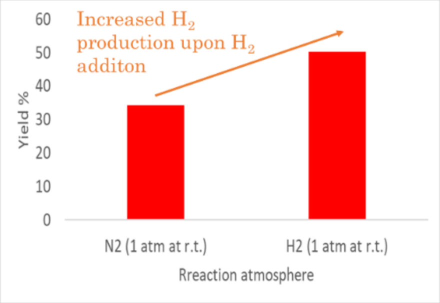

*Figure 1: Hydrogen production by PtNi catalyst under nitrogen and hydrogen atmosphere*

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# Rational optimisation of biomass-derived γ-valerolactone cascade synthesis

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## Abstract

To fully investigate a complex system, which depends on the interplay between numerous independent variables, traditional approaches often fall short. Relying on the one-variable-at-a-time approach, the interaction between variables is impossible to observe, much less quantify. In this context, a rational Design of Experiment (DoE) allows more efficient and thorough exploration of the experimental domain.[1] This approach was applied to the synthesis of γ-valerolactone (GVL) from biomass-derived furfuryl alcohol (FAL), a complex one-pot, multi-step process which hinges on the successful combination of two catalyst functionalities, the appropriate catalyst loading, substrate concentration and reaction time and temperature.[12]

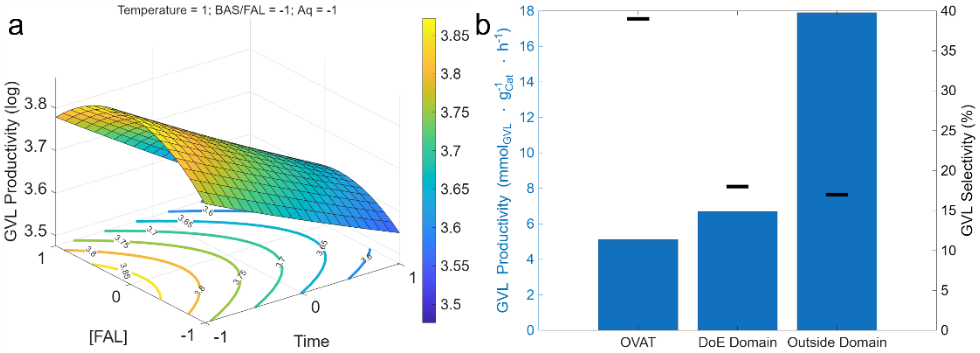

*Figure 14: a) GVL productivity response surface and b) results of the optimization of the process.*

A 5-variables faced central-composite design was employed, resulting in 50 tests being carried out to explore the experimental domain and estimate experimental variance through the repetitions of some experiments. The investigation not only allowed a thorough understanding of this complex reaction system through the study of the regression coefficients and the response surfaces (Figure 1a), but also provided actionable insight, which guided further experimentation, resulting in an unprecedented GVL productivity of 18 $\text{mmol}_{GVL}/\text{g}_{Cat}/\text{h}$ (Figure 1b), which amounts to a 250% increase compared to the starting point of the study.

**Keywords**: Design of Experiment, Heterogeneous Catalysis, GVL

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