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Research Article

Exosomes: From Basic Biology to Clinical Utilization

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Exosomes were first recognized in the early 1980s during studies of reticulocyte maturation, where small vesicles were shown to remove unwanted membrane proteins such as the transferrin receptor via multivesicular body (MVB)-mediated release.[1,2] Johnstone and colleagues later coined the term "exosome" (1987), initially viewing them as a cellular disposal pathway.[3] In the mid-late 1990s, landmark immunology studies revealed that exosomes from antigen-presenting cells carry functional MHC molecules and can activate T cells, reframing exosomes as active mediators of intercellular communication rather than cellular waste. In this article, we will further summarize the recent progress on basic biology of exosomes as well as their clinical applications and considerations.

Exosome Biogenesis

Exosomes are a subtype of extracellular vesicles (EVs). They are nanoscale, phospholipid bilayer enclosed vesicles typically ~30-200 nm in diameter that are released by almost of all cell types.[4,5] Exosomes originate from the endocytic system. Following endocytosis, early endosomes mature and interact with intracellular compartments (e.g., the trans-Golgi network and endoplasmic reticulum), during which specific biomolecules are sorted into the endosomal lumen. Inward budding of the endosomal membrane generates intraluminal vesicles (ILVs) within multivesicular bodies (MVBs). When MVBs fuse with the plasma membrane, ILVs are released into the extracellular space; these released ILVs are commonly referred to as exosomes.[5,6]

Exosome-Mediated Cell–Cell Communication

As shown in **figure 1**, exosomes can act as carriers of biological information across short and long distances through biofluids (e.g., blood, urine, saliva, milk).[7,8,9] Recipient cells may interact with exosomes through (i) receptor–ligand interactions at the cell surface, (ii) multiple endocytic routes (including clathrin-mediated uptake, caveolin-mediated uptake, macropinocytosis, and phagocytosis), and (iii) in some contexts, direct membrane fusion.[4,10] Beyond direct cellular uptake, exosomes may also remodel local microenvironments by depositing cargo in the extracellular space, contributing to sustained signaling effects.[11]

Exosomes contain diverse cargo, including proteins (such as enzymes, signal proteins, transcriptional factors etc.), lipids (e.g. ceramides), and nucleic acids (mRNA as microRNA, long-non-coding RNA as lncRNA, circular RNA as circRNA, and occasionally DNA), as well as bioactive molecules such as cytokines and growth factors.[4,5,7] Delivery of these cargo molecules can alter signaling pathways and gene expression in recipient cells, leading to functional or phenotypic changes. Exosomes are therefore implicated in a broad range of physiological and pathological processes, including immune regulation, tissue repair, cancer progression, cardiovascular disease, and central nervous system disorders.[4,5] Because exosomes can protect cargo within a lipid bilayer and facilitate delivery to target cells, they have attracted significant interest as potential therapeutic agents and drug delivery vehicles.[12]

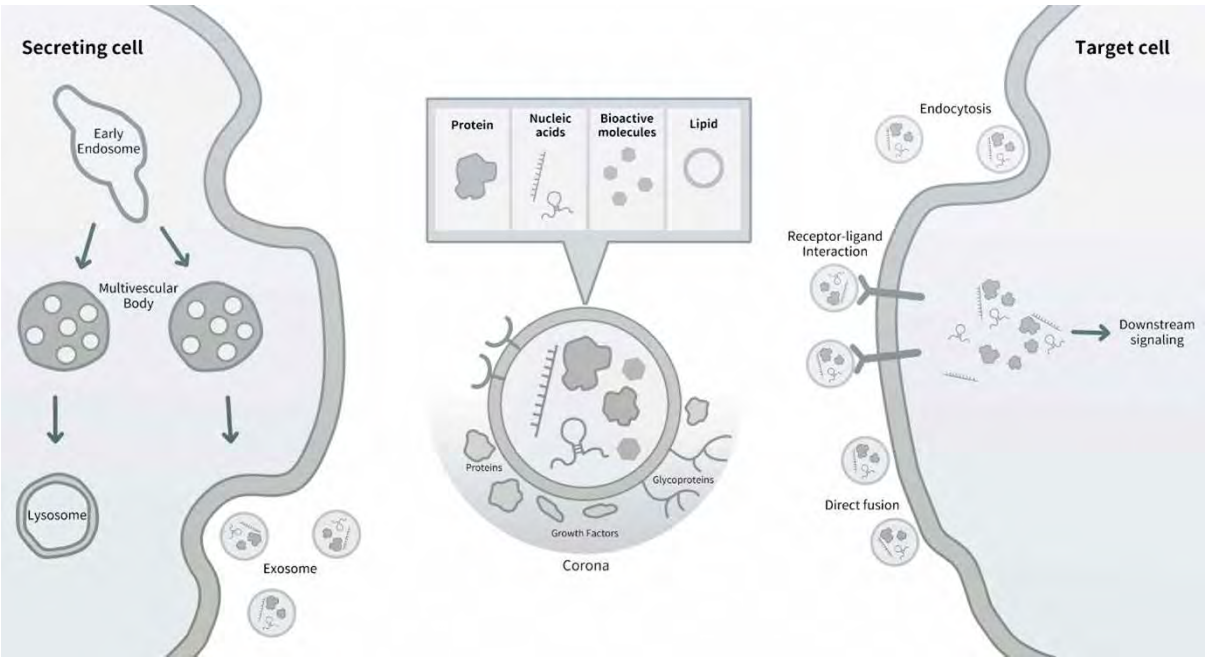


Figure 1. Exosome biogenesis, cargo composition, and uptake mechanisms driving intercellular signaling

Schematic overview of exosome-mediated cell-cell communication. In the secreting cell (left), early endosomes mature into multivesicular bodies (MVBs) containing intraluminal vesicles; MVBs either fuse with lysosomes for degradation or with the plasma membrane to release exosomes into the extracellular space. Released exosomes carry diverse cargo classes—including proteins, nucleic acids, bioactive molecules, and lipids (top inset). Upon release, exosomes can adsorb extracellular components (e.g., proteins, glycoproteins, growth factors), forming a biomolecular "corona" that may influence stability and interactions with recipient cells (center). In target cells (right), exosomes elicit downstream signaling via multiple routes, including endocytosis, receptor–ligand interactions at the cell surface, and direct membrane fusion, leading to delivery of cargo and modulation of cellular responses.

Sources of Exosomes and Functional Diversity

Exosomes (and other EVs) are produced by many organisms and cell types. EV-like particles have been reported from mammalian cells, plants, and microbes, and EVs can be isolated from many biofluids and artificial culture systems. Importantly, exosomes from different sources can differ substantially in composition and function.

For example, stem cell-derived exosomes have been widely investigated for regenerative and immunomodulatory properties, with reported effects in contexts such as wound healing and tissue repair.[13] Blood- and/or Urine-derived exosomes have been explored as non-invasive biomarker sources, since their cargo may reflect physiological or disease states.[14] Plant-derived EVs have been reported to exhibit antioxidant and anti-inflammatory activities in some experimental settings.[15] Immune cell–derived exosomes, such as those from dendritic cells, have been studied for their ability to modulate immune responses, including potential anti-tumor immunity.[16] Milk-derived exosomes (MDEs) have also been examined for roles in intestinal homeostasis and nutritional health,[5] with studies suggesting protective effects against certain dietary or environmental stressors.

Exosome Isolation and Purification

A key practical question is how to isolate exosomes with sufficient yield and purity. Several commonly used approaches include[8] as well as summarized in **figure 2**:

1. Differential ultracentrifugation
   Sequential centrifugation steps at increasing speeds are used to pellet larger debris first and enrich smaller vesicles later. This method is widely used but may yield preparations with variable purity due to co-isolation of non-vesicular components.
2. Density gradient ultracentrifugation
   Gradients (e.g., sucrose or iodixanol) separate particles by buoyant density, improving purity compared with

differential ultracentrifugation, though the method can be time-consuming.

3. Ultrafiltration (e.g., tangential flow filtration, TFF)
   Size-based membrane filtration retains particles above a defined pore size or molecular weight cutoff. TFF is often used for scalable processing and can be compatible with large-volume production.
4. Polymer-based precipitation (e.g., PEG precipitation)
   Polyethylene glycol reduces solubility and promotes precipitation of extracellular particles under lower-speed centrifugation. This approach is convenient but can co-precipitate proteins and other contaminants, often requiring downstream cleanup.

In practice, isolation strategies are frequently combined (e.g., filtration plus chromatography or density-based steps) to balance functionality, yield, purity, scalability, and cost.

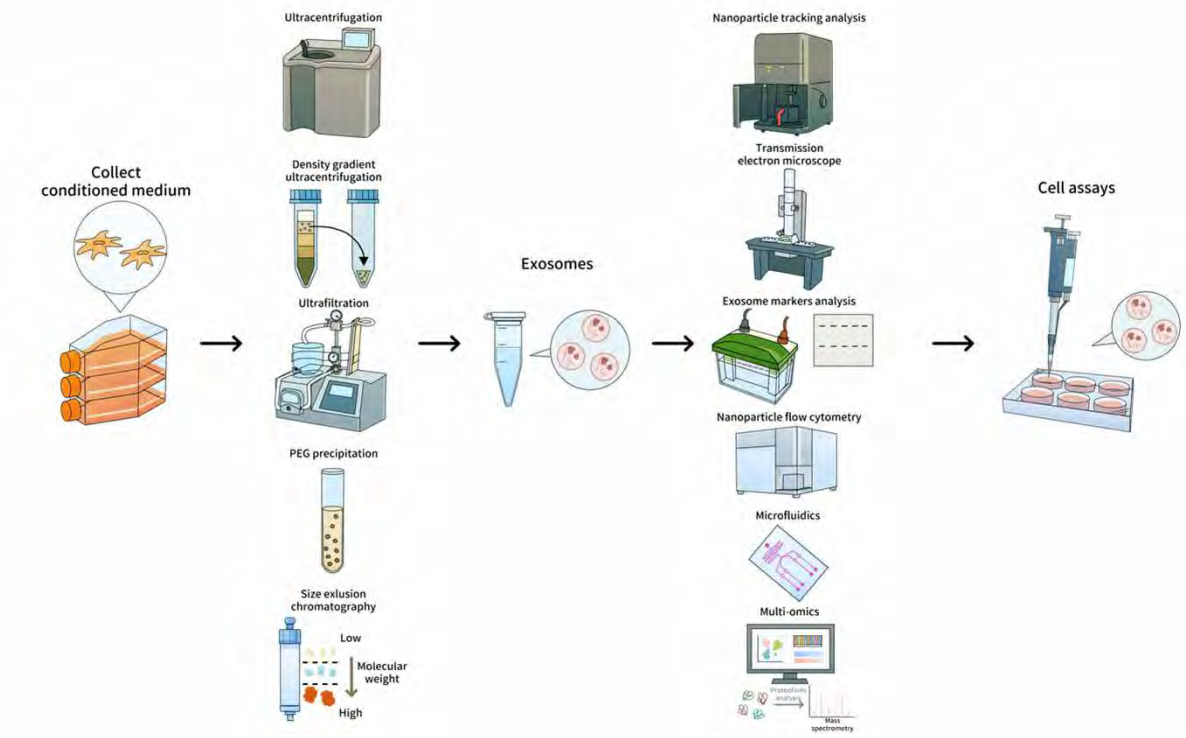


Figure 2. Workflow for exosome isolation, characterization, and functional evaluation from conditioned media

Schematic pipeline illustrating common steps used to obtain and evaluate exosomes from cell culture conditioned medium. Conditioned medium is first collected from cultured cells (left) and subjected to exosome isolation/enrichment using one or more approaches, including differential ultracentrifugation, density gradient ultracentrifugation, ultrafiltration (e.g., tangential flow filtration–based concentration), polymer-based precipitation (e.g., PEG), and size exclusion chromatography (middle). The resulting exosome preparation (center) is then characterized using complementary analytical methods (right), such as nanoparticle tracking analysis (NTA) for particle size and concentration, transmission electron microscopy (TEM) for vesicle morphology, and exosome marker analysis (e.g., immunoblot or immunoassays) to support identity assessment. Additional platforms—including nanoparticle flow cytometry, microfluidic-based enrichment/analysis, and multi-omics profiling (proteomics, transcriptomics, lipidomics)—can further define vesicle subpopulations and cargo composition. Finally, functional activity is evaluated in downstream cell-based assays (far right) to link exosome properties to biological effects in a fit-for-purpose manner.

Multi-Omics Profiling of Exosomes

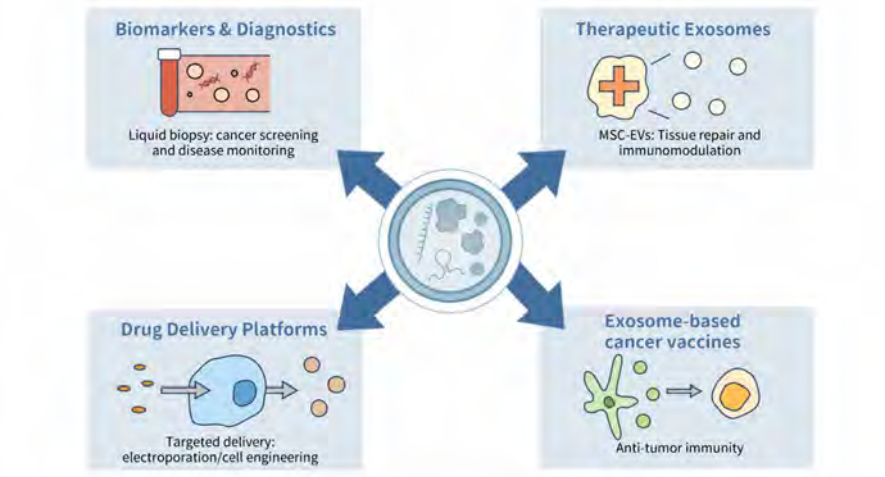
After isolation, exosomes can be characterized using multi-omics approaches to define their cargo and infer functional roles. Proteomics can identify functional protein components, reveal cargo-sorting patterns, and suggest candidate biomarkers. Transcriptomics can profile RNA species within exosomes—including miRNAs and other non-coding RNAs—many of which are relatively stable due to protection by the lipid bilayer. Lipidomics and metabolomics can further characterize bioactive lipid species and metabolic signatures.[11]

Compared with single-analyte measurements, multi-omics provides a systems-level view of exosome biology. Integrating omics data with pathway analysis and curated databases can help predict interactions between exosomes and recipient cells and identify diagnostic or therapeutic opportunities. In oncology in particular, exosome-derived biomarkers have been actively explored for early detection, prognosis, and treatment monitoring.

Clinical and Translational Applications

Exosomes have several major translational directions[11] as shown in **figure 3** and below:

1. Biomarkers and diagnostics
   Because exosomes are present in many biofluids and can protect molecular cargo from degradation, they are attractive sources for minimally invasive biomarkers. Exosomal RNA, DNA-associated signals, and protein markers have all been investigated, especially for cancer diagnosis and prognosis.
2. Therapeutic exosomes
   Increasing interest has focused on mesenchymal stromal cell–derived extracellular vesicles (MSC-EVs) due to reported immunomodulatory and regenerative properties. Clinical research has explored MSC-EVs in areas such as tissue repair and inflammatory conditions, among others.
3. Drug delivery platforms
   Exosomes can potentially act as delivery vehicles due to their membrane structure and cell interaction mechanisms. Cargo loading strategies are often described as: (1) Direct loading, in which therapeutic agents are introduced into isolated exosomes (e.g., by electroporation or co-incubation), and (2) Indirect loading, in which parent cells are engineered or treated so that secreted exosomes contain desired cargo.[9]
4. Exosome-based cancer vaccines
   Exosomes from immune cells or tumor-associated sources have been studied for their potential to stimulate anti-tumor immune responses. While promising, this area still requires extensive validation and safety assessment.[9]



Comparisons of Exosome Loading Strategies

Strategy	Pros	Cons
Direct Loading Post-isolation processing, high cargo capacity, broad cargo range (drugs, genes)	High loading efficiency, controllable release, versatility in cargos, enhanced therapeutic effect	Membrane damage, inconsistency, strict conditions
Indirect Loading Maintain cell integrity, scalable by cell culture	High biocompatibility, crossing biological barriers, cargo protection, ideal for loading miRNA and proteins	Production challenges (purity and yield), release control

Figure 3. Different clinical and translational applications of exosomes

The schematic illustration (top) highlights four primary domains of exosome application in clinical applications: (1) Biomarkers and diagnostics: utilized in liquid biopsy for cancer screening and disease monitoring; (2) Therapeutic exosomes: specifically mesenchymal stem cell-derived extracellular vesicles (MSC-EVs) for tissue repair and immunomodulation; (3) Drug Delivery Platforms: exosomes can act as delivery vehicle, by employing targeted delivery techniques such as electroporation and cell engineering; and (4) Exosome-based cancer vaccines: designed to elicit anti-tumor immunity. The table summarizes the advantages and limitations of two distinct exosome cargo loading approaches: Direct loading and indirect loading, comparing the advantages and disadvantages of the two different loading strategies.

Manufacturing process and considerations

For industrial translation, exosome development should be framed as a manufacturing and quality system rather than a purely biological phenomenon. A practical end-to-end workflow begins with **source definition and controlled collection**, in which the origin (e.g., producer cell line, milk, biofluid, or plant material) is clearly specified with traceability and acceptance criteria, and harvest variables such as temperature, time-to-processing, and storage/hold conditions are standardized; for culture-derived products, upstream controls further include media composition, culture duration, and stress conditions that can shift EV yield and cargo profiles. The process then proceeds through clarification, typically using low-speed centrifugation and/or depth filtration to remove cells and debris, often coupled with pre-filtration to minimize fouling of downstream membranes or chromatographic media. Concentration and buffer exchange are commonly implemented by ultrafiltration or tangential flow filtration (TFF), enabling scale-up while exchanging into formulation-compatible buffers; at this stage, recovery should be tracked and processing stresses (e.g., high shear or transmembrane pressure) minimized to preserve vesicle integrity.[17] Downstream purification/polishing is selected based on the source matrix and is directed toward reducing free proteins, aggregates, lipoproteins, and other co-isolated nanoparticles; importantly, improvements in purity should be confirmed using orthogonal analytical methods rather than relying on a single marker readout.[18] Finally, formulation and fill/finish require defining a pH and ionic-strength window that maintains vesicle stability, establishing packaging and cold-chain requirements when necessary, and implementing a stability program;[19] conventional 0.22 μm sterile filtration is often unsuitable because it can remove or damage vesicles, so microbial control is typically achieved through low-bioburden processing, closed handling where appropriate, and fit-for-purpose microbiological testing (particularly critical for therapeutic platforms). Across these steps, industrialization depends on a predefined set of critical quality attributes (CQAs) spanning identity (particle size distribution and concentration measured by tools such as NTA, complemented by a multi-assay marker strategy), purity (total protein and a protein-to-particle metric as an operational purity index, plus source-specific contaminant monitoring such as lipoproteins or matrix proteins), potency (a fit-for-purpose bioassay aligned to the intended use—e.g., barrier support or stress-response endpoints for topical applications—anchored to an internal reference batch to detect drift), safety (bioburden/sterility strategy appropriate to product class, residual process reagents, and mycoplasma/endotoxin where relevant), and stability (real-time and accelerated plans with trending of size, concentration, and potency surrogates over time). These elements should culminate in batch-by-batch release documentation via a Certificate of Analysis (COA) that records lot information and storage conditions, reports quantitative release tests (size, concentration, protein, purity proxy, and identity marker panel), includes potency relative to a reference, and documents safety tests and final disposition (released, conditional release, or rejected). Taken together, this manufacture architecture operationalizes exosomes as a manufacturable bioactive ingredient, reduces batch disputes, strengthens partner confidence, and provides a foundation for credible commercialization.

Current Challenges and Future Directions

Despite their potential, several challenges remain before exosome-based applications become routine: [6,7,9,13]

1. Standardization and reproducibility
   Exosome preparations can be heterogeneous in size, cargo, and biological activity. Establishing standardized manufacturing and quality control (QC) criteria is essential.
2. Incomplete understanding of basic biology
   While broad mechanisms of biogenesis and uptake are known, many details of cargo selection, trafficking, and functional delivery remain unclear.
3. Purity and co-isolated contaminants
   Exosomes often co-exist with non-vesicular extracellular nanoparticles, protein aggregates, and lipoproteins in biofluids. Many isolation methods co-enrich these components, complicating interpretation and downstream use. Moreover, commonly used markers such as CD9, CD63, and CD81 do not capture all exosome subpopulations, so robust characterization typically requires multiple orthogonal assays.
4. Scalable manufacturing and GMP compliance
   Achieving high-yield, large-scale production under standardized conditions remains challenging. For drug delivery applications, loading methods may affect vesicle integrity or alter exosome properties, creating additional QC burdens.
5. In vivo tracking, biodistribution, and pharmacokinetics
   Methods to track exosomes and quantify delivery efficiency in vivo are still developing. Exosomes may be cleared rapidly by the mononuclear phagocyte system, reducing effective delivery to target tissues.
6. Safety considerations
   Although exosomes are often perceived as “natural,” their safety profiles must be evaluated carefully. For example, MSC-EVs may have context-dependent effects, and some studies suggest possible pro-tumorigenic risks under certain conditions. Rigorous safety testing is therefore essential.

Conclusion

Exosomes represent a rapidly evolving class of biological nanoparticles with promising applications in diagnostics, therapeutics, and drug delivery. However, translation requires continued advances in mechanistic understanding, isolation and manufacturing technologies, potency assays, and standardized QC frameworks. With careful development and evidence-based evaluation, exosomes may become an important component of future biomedical and biotechnology innovations.

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Author Information

Zhen-Yi Li was born in 2001 in Taipei, Taiwan. She completed her undergraduate studies at National Taiwan University. She is now studying for a master's degree in the laboratory of Professor Tang-long Shen (National Taiwan University), where she is doing research in the field of cancer-related exosomes.

Jiamei Liu received her Master degree from the Institute of Microbiology and Immunology, National Yang Ming Chiao Tung University (Taiwan) in 2023, under the supervision of Professor Chuen-Miin Leu. Since 2025, she has been working in the laboratory of Professor Tang-Long Shen, Department of Plant Pathology and Microbiology, National Taiwan University (Taiwan).

Tang-Long Shen is a Professor in the Department of Plant Pathology and Microbiology, National Taiwan University (NTU). He earned his B.S. (1987–1991) and M.S. (1992–1994) at NTU, and completed his Ph.D. in Molecular Medicine at Cornell University (1997–2002). After returning to NTU, he joined the faculty in 2004, serving as Assistant Professor (2004–2011) and Associate Professor (2011–2016), and has since held senior leadership roles including Director of the Center for Biotechnology (from 2016) and Director of the NTU GIP-TRIAD International Joint Degree Master's Program in Agro-biomedicine in Food and Health (from 2021). Prof. Shen's research centers on cell signaling and cancer biology, with emphasis on integrin and growth factor signaling, cancer cell biology (including tumor exosomes), molecular plant–microbe interactions such as RNA silencing and viroid biology, and secondary metabolites of medicinal fungi such as Cordyceps spp. In addition to his academic work, he has been active in Taiwan's extracellular vesicle community, including leadership roles associated with the Taiwan Society for Extracellular Vesicles (TSEV).

Related Products

Exosome Isolation Reagent [for Serum]	1.5mL	E1553
Exosome Isolation Reagent [for Cell Culture Media]	25mL	E1601

Chemistry Chat

Polysulfide Anions Photoredox Catalysis

Nanyang Technological University Singapore

Shunsuke Chiba, Professor

Since joining Nanyang Technological University (NTU Singapore), one of the public universities in Singapore, in April 2007, I have been engaged in the development of synthetic organic reactions and the total synthesis of complex natural products. Our research style for reaction development is to plan and conduct daily experiments based on a broad hypothesis, while also accurately capturing and shaping unexpected and unidentified phenomena (reactivity) that suddenly appear without warning. This is a research approach I learned from Prof. Koichi Narasaka when I studied as a graduate student and worked as a research associate in his group.[1] Capturing these opportunities, which may arise at any time, requires not only basic knowledge to determine whether they are scientifically interesting, but also careful tracking of any reaction and a commitment to thorough pre- and post-processing checks. This is not an easy task. However, when the reactivity discovered in this way turns out to be a completely new and previously unknown one, the time spent developing it into a research topic is truly rewarding. In this essay, I would like to introduce the development of photoredox catalysis using polysulfide anions, one of the current main research themes in our group at NTU Singapore, from a chance encounter with polysulfide anions to the development of this research theme.

In 2019, our group had the opportunity to collaborate with pharmaceutical companies based in Singapore. The project involved improving several molecular transformations to be performed under reaction conditions suitable for API manufacturing (e.g., environmentally friendly conditions, transition metal-free, suitable for continuous flow settings, etc.). One of the reactions selected was the cross-coupling of aryl halides with heteroaromatic compounds such as pyrroles (**Figure 1**). In fact, the resulting heterobiaryl motifs are used as the main skeletons of various pharmaceutical and agrochemical active ingredients.

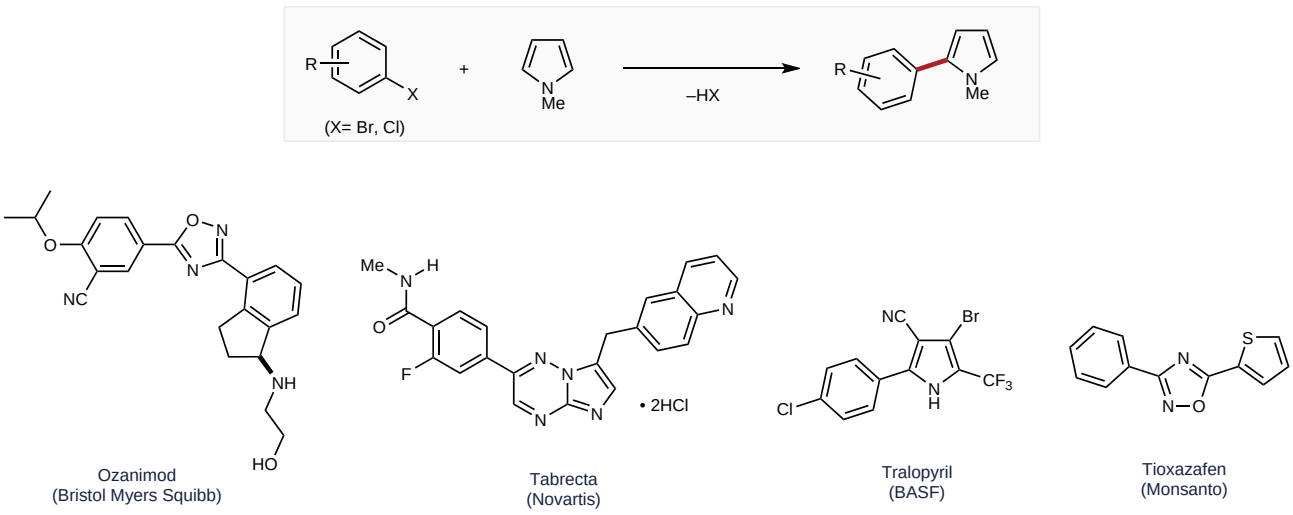


Figure 1

Having long been involved in radical reactions driven by single-electron transfer (SET), I sought to apply SET to this project as well. Considering the cross-coupling reaction of aryl halides and pyrrole based on the concept of "electron catalysis"[2,3] proposed by Prof. Eiji Shirakawa (Kwansei Gakuin University), Prof. Dennis Curran (University of Pittsburgh), and Prof. Armido Studer (University of Münster), we can consider this reaction as a redox-neutral reaction mechanism, as shown in **Figure 2**. First, one electron is injected into the aryl halide (single-electron reduction), generating an aryl halide radical anion, which then induces mesolytic cleavage of the carbon-halogen bond to generate an aryl radical. The resulting aryl radical then adds to pyrrole to form a radical adduct, which then undergoes one-electron removal (single-electron oxidation) and deprotonation to yield a heterobiaryl compound. If the electron released from the system could be injected into the next aryl halide, the single electron-catalytic cycle would be maintained, but in reality, this does not always work. Here, we must consider the ease of electron injection into the aryl halide (reduction potential) and the ease of electron removal from the radical adduct (oxidation potential). The reduction potential of the aryl halide is generally below –2 V vs. SCE, while this is affected by the substituents on the aryl group. This requires a strong electron injection ability (reducing ability) to enable electron injection. On the other hand, assuming that the single-electron oxidation to produce the biaryl occurs from the radical adduct prior to deprotonation, the oxidation potential of the analogous α-amino radical to iminium is approximately –0.9 V vs. SCE. Therefore, the reduction-oxidation energy barrier in this single-electron catalytic cycle is greater than 1 eV (23 kcal/mol), requiring efficient energy input to compensate for this.

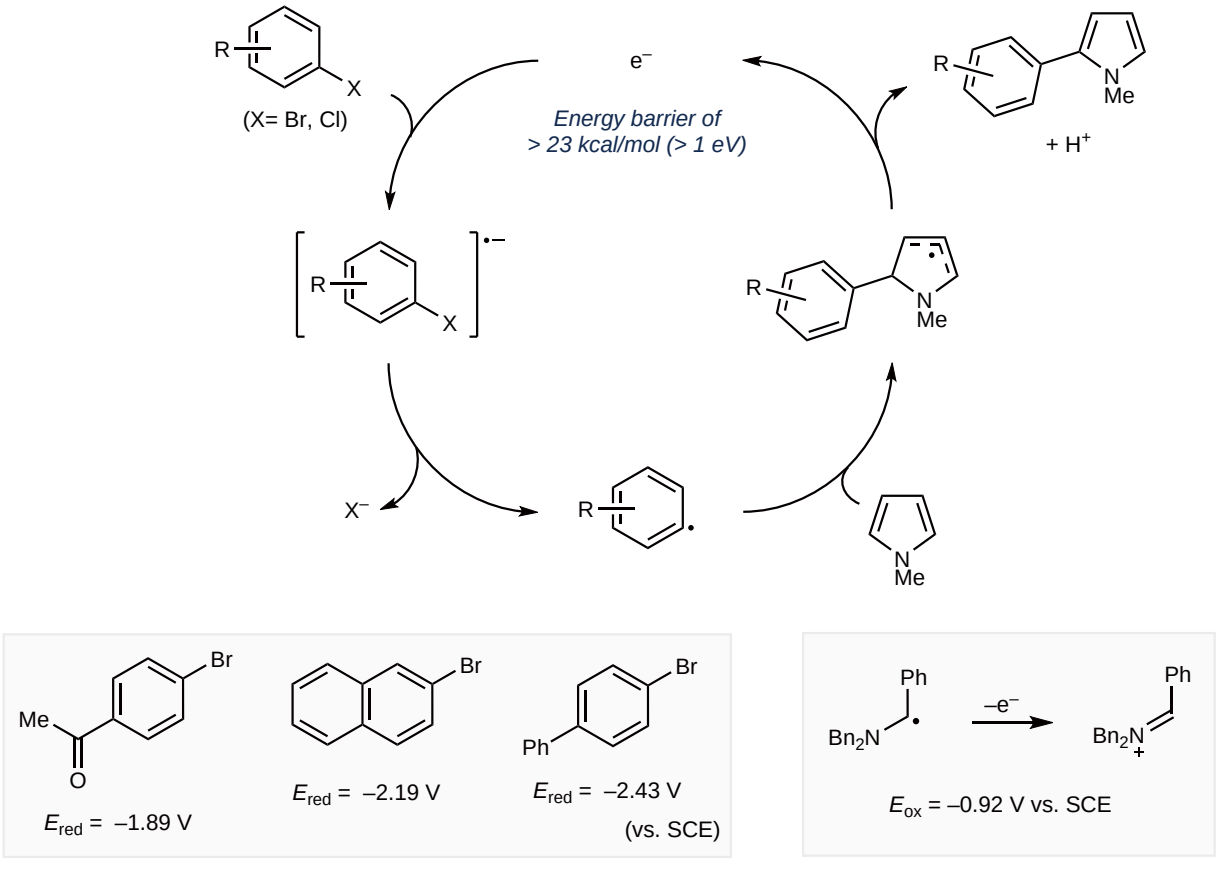


Figure 2

Recently, photoredox catalysis, primarily driven by visible light, has emerged as a method to overcome the energy barrier of redox reactions. Since various photoredox catalysts have been reported to be capable of carrying out this biaryl cross-coupling reaction (**Figure 3**), we were initially optimistic that we could use one of these catalysts and optimize the reaction conditions for scale-up. However, these catalytic reactions generally require long reaction times of 24-72 hours. Presumably, the return to the original system via the one-electron oxidation (back electron transfer) of the radical anion that occurs simultaneously with the one-electron reduction of the aryl halide slows down the catalytic cycle. Naturally, this characteristic makes them unsuitable for the scale-up. Given this backdrop, we decided to explore new reaction conditions that would enable a "rapid" cross-coupling reaction that would be suitable for scale-up, together with a postdoctoral fellow, Dr. Haoyu Li (currently Professor at Great Bay University).

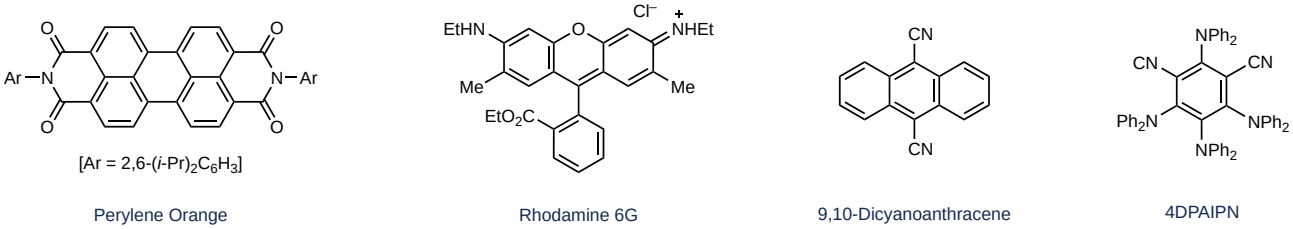


Figure 3

We decided to first search the literature for coupling reactions of aryl halides via aryl radicals that could proceed at a fast reaction rate. Our attention was drawn to the cross-coupling of aryl halides with thiols reported in 2017 by Prof. G. Miyake at Colorado State University (**Figure 4**).[4] This cross-coupling does not require any catalysts and proceeds under mild conditions at ambient temperature, using only a base such as cesium carbonate and visible light irradiation. Interestingly, the reaction is very fast, completing within a few hours in the case of bromoarenes. According to the proposed reaction mechanism, the process is initiated by inner-sphere electron transfer upon visible light excitation of an electron-donor-acceptor (EDA) complex between a thiolate and an aryl halide. The sulfur radical and aryl radical pair formed within the solvent cage then couple directly to yield the product.

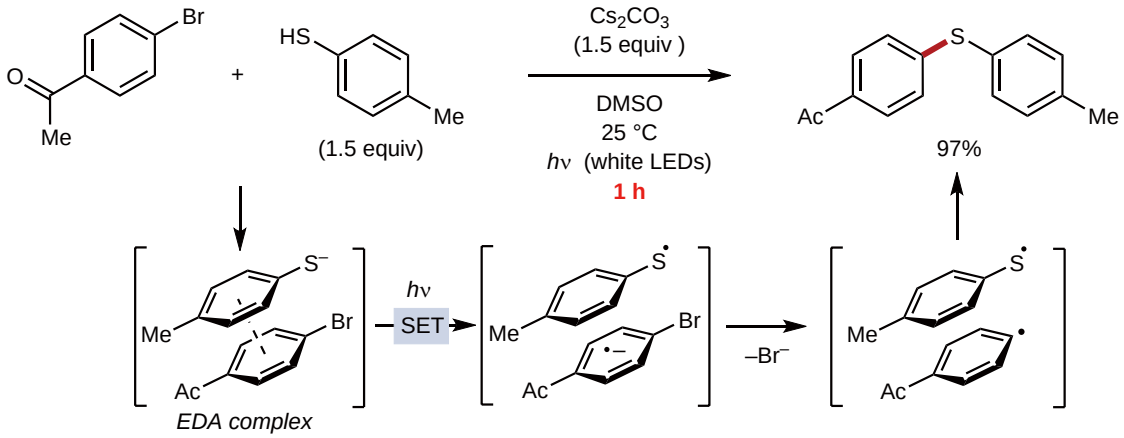


Figure 4

This reaction rapidly generates aryl radicals from aryl halides, which can then be used in cross-coupling. To apply this feature to our desired biaryl cross-coupling, we hypothesized the following (**Figure 5**): a bulky thiol such as triisopropylsilanethiol is used, and visible light excitation of the EDA complex induces inner-sphere electron transfer, resulting in the radical anion of the aryl halide and a sulfur radical, which then diffuse rapidly out of the solvent cage due to steric repulsion. The subsequently generated aryl radical is then captured by pyrrole, which is coexisting in the system.

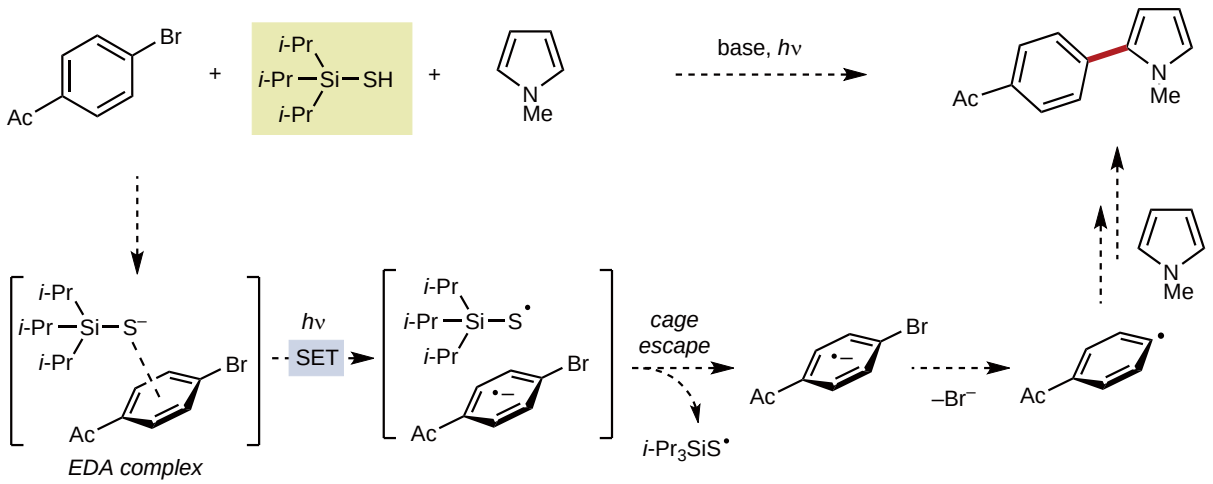


Figure 5

In fact, when a DMSO solution of 4-bromoacetophenone and pyrrole was irradiated with blue light in the presence of a catalytic amount of triisopropylsilanethiol and potassium carbonate, the reaction proceeded very quickly (1.5 hours), providing the desired cross-coupled product in high yield (**Figure 6**). Mission accomplished! Just as we were celebrating, Haoyu reported that no triisopropylsilanethiol was recovered after the reaction (it disappeared immediately after the reaction began) and, strangely, the reaction solution immediately took on a beautiful blue-green color after irradiation. This left us with questions about whether the reaction was proceeding according to our hypothesized mechanism.

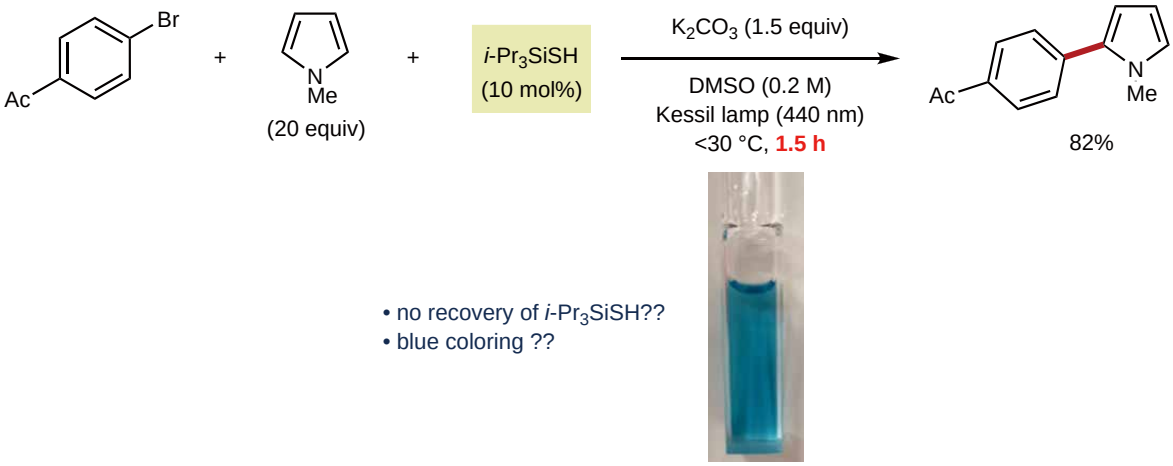


Figure 6

Actually, 4-bromoacetophenone, pyrrole, and triisopropylsilanethiol used in the reaction were all colorless, transparent liquids with no visible light absorption. However, when potassium carbonate was added to a DMSO solution of triisopropylsilanethiol, the mixture immediately turned blue-green, similar to the reaction mixture (**Figure 7**). This suggested that something with a visible absorption band was produced from triisopropylsilanethiol, and we realized that this was polysulfide anions after some struggles. A DMSO solution of commercially available potassium polysulfide (K_2S_x) also turned blue-green, revealing the role of S_4^{2-}, S_6^{2-}, and $S_3^{\bullet-}$, which have visible light absorption bands. We believe that under basic conditions, triisopropylsilanethiol is oxidized by the DMSO solvent to the corresponding disulfide, which then undergoes complex disproportionation, triggered by desilylation, to reach an equilibrium state of a mixture of various polysulfide anions. By the way, we occasionally see reactions in which triisopropylsilanethiol is used as a polarity reversal catalyst in radical reactions, but we might be cautious of its behavior, especially in reaction systems under redox settings.

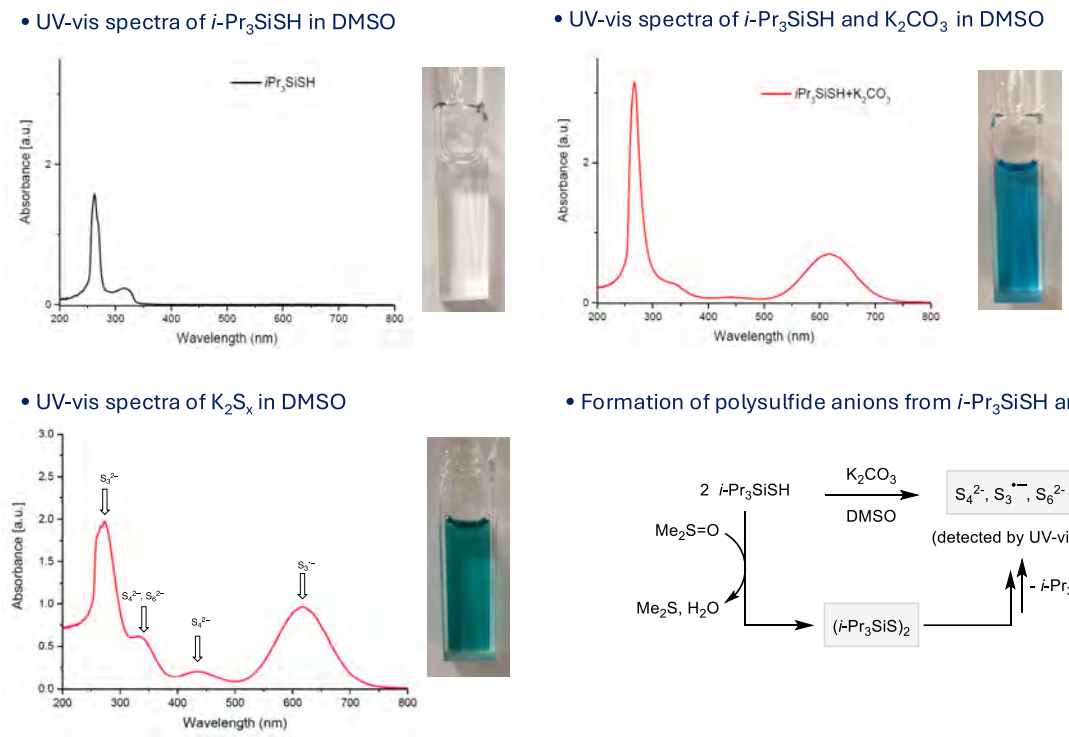


Figure 7

Polysulfide anions are reactive intermediates at the cathode of lithium-sulfur batteries, and their redox potentials have been extensively investigated.[5] The redox potentials of the $S_4^{2-}/S_4^{\bullet-}$ and $S_6^{2-}/S_6^{\bullet-}$ redox pairs are –0.85 V vs. SCE and –0.4 V vs. SCE, respectively. Because these pairs absorb visible light in the blue-violet region, we hypothesized that the excited species of S_4^{2-} and S_6^{2-} might act as single-electron reductants for aryl halides. Indeed, when a DMSO solution of 4-bromoacetophenone and pyrrole was irradiated with blue light in the presence of a catalytic amount of potassium polysulfide (K_2S_x) and potassium carbonate, the desired heterobiaryl cross-coupled coupling proceeded rapidly (**Figure 8**).[6]

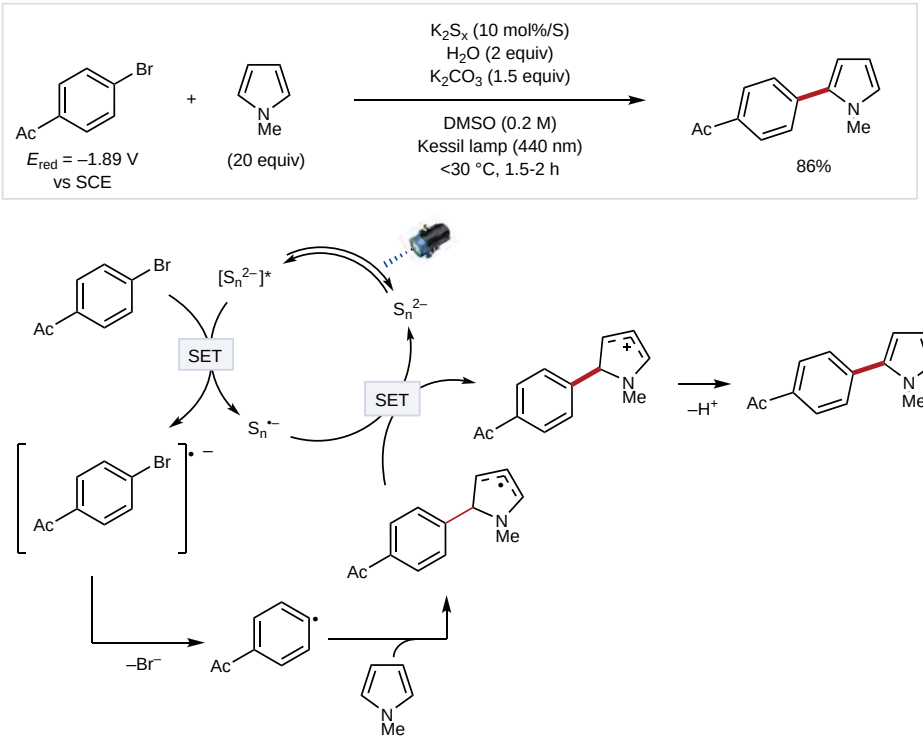


Figure 8

Thus, we found that polysulfide anions can be used as very unique photoredox catalysts. Potassium polysulfide is far less expensive than commonly used photoredox catalysts, which is another factor that makes it useful in practical chemical synthesis. We also demonstrated that this catalytic system can be applied to the Miyaura-type borylation, with pinacoldiborane as an aryl radical scavenger for the cross-coupling of aryl halides, and the hydroarylation of alkenes (**Figure 9**).[7]

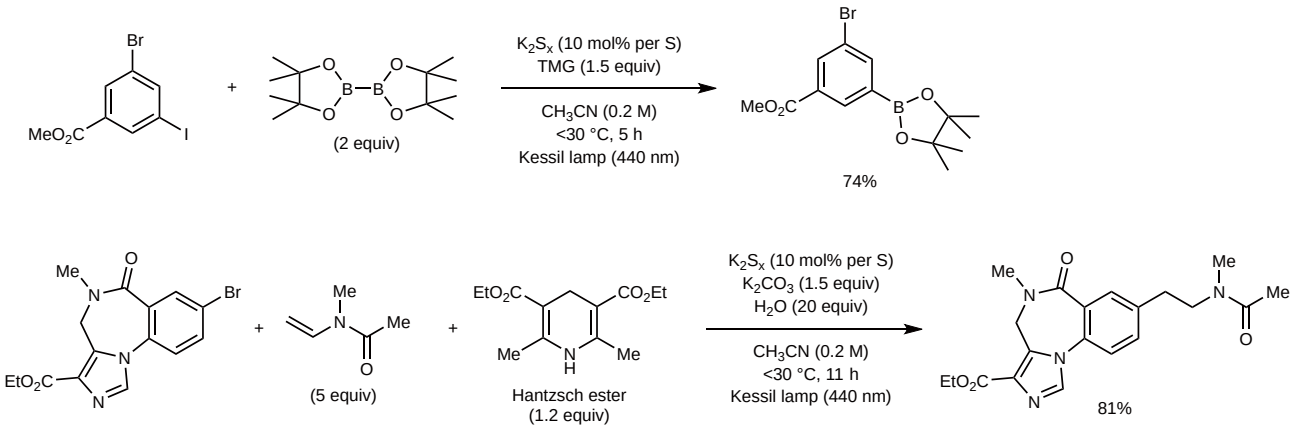
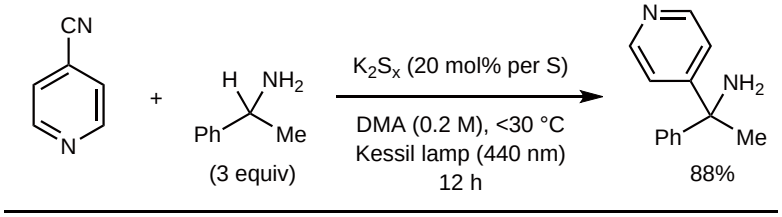


Figure 9

Photoredox reactions using polysulfide anions can also be applied to the C-H functionalization of benzylamines.[8] For example, when a mixture of 4-cyanopyridine and benzylamine is irradiated with blue light in the presence of a catalytic amount of potassium polysulfide, pyridine is introduced at the benzylic position of benzylamine (**Figure 10**). The 4-cyanopyridine radical anion generated by single-electron reduction is persistent. At the same time, the polysulfide radical anion abstracts a hydrogen atom at the benzylic position of benzylamine (HAT), generating a transient benzyl radical. This radical then cross-couples with the previously generated 4-cyanopyridine radical anion at a rate nearly limited by diffusion to give the product.[9]



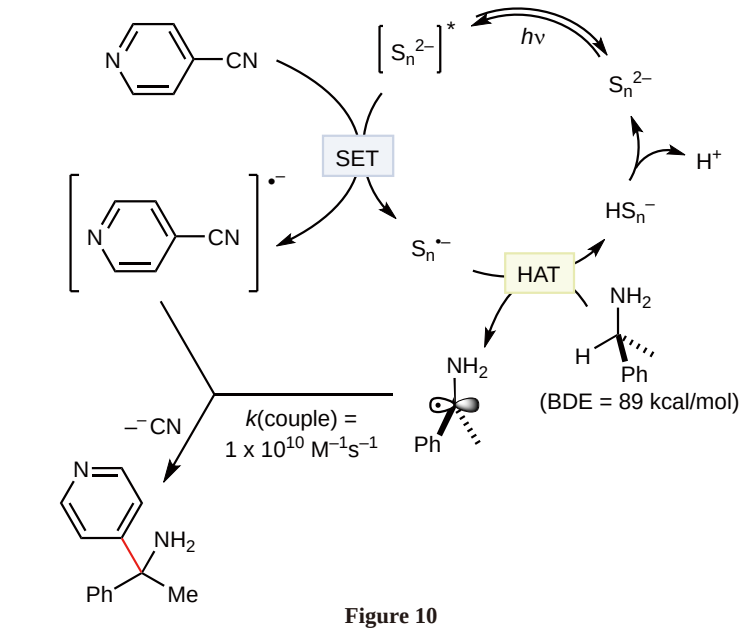


Figure 10

Thus, it has been found that the polysulfide radical anions generated by one-electron reduction with excited polysulfide anions not only act as a mild one-electron oxidant, but also have the reactivity to induce HAT with relatively electron-rich carbon-hydrogen bonds (**Figure 11**). For example, potassium formate can be used as a HAT partner. In this case, the carbon dioxide radical anion (E_{ox} = –2.3 V vs. SCE) generated together with the polysulfide anion regenerated by HAT also acts as a very strong single-electron reducing agent, so a synergistic effect can be expected that further promotes the target reduction reaction.

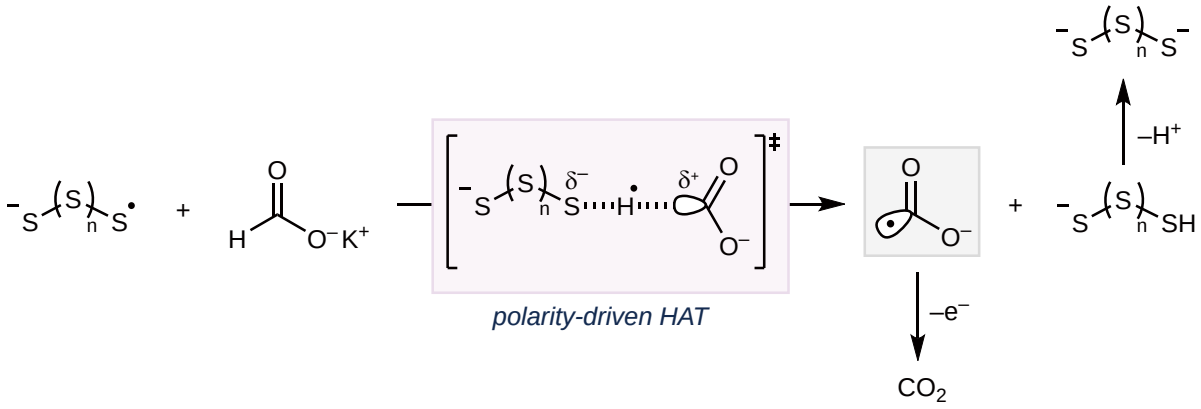


Figure 11

For example, photoreduction using a combination of potassium polysulfide and potassium formate is effective for the desulfonylation of sulfonamides (**Figure 12**).[10] It is known that primary amine sulfonamides act as excellent nucleophiles under basic reaction conditions, efficiently giving secondary amine sulfonamides through nucleophilic substitution reactions with various haloalkanes or the Mitsunobu reactions with alcohols. However, the removal of the tosyl group commonly requires harsh acidic or basic reaction conditions, which is a drawback from a practical standpoint. On the other hand, our system can efficiently remove tosyl and even mesyl groups from arylalkylamines and dialkylamines under relatively milder reaction conditions: in the presence of catalytic amounts of potassium polysulfide and potassium formate, in DMSO, and under irradiation with violet light.

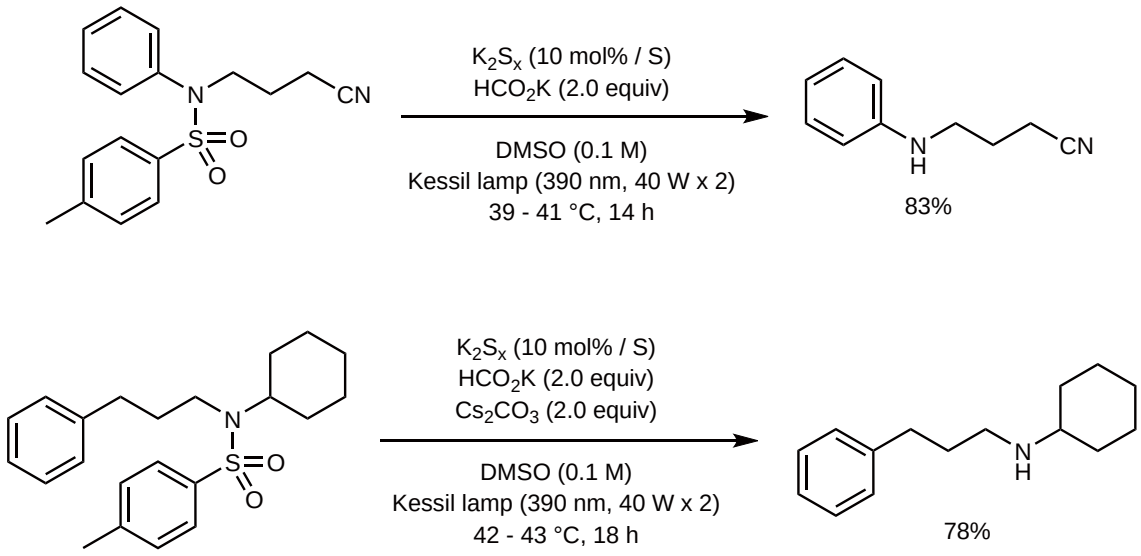


Figure 12

Furthermore, photoreduction conditions using a combination of potassium polysulfide and potassium formate can also be used for the dearomatization of naphthalenes and indoles via a Birch-type reduction (**Figure 13**).[11] Interestingly, when these photo-Birch-type reduction conditions are applied to 4-arylquinolines, the quinoline skeleton is converted to an indole, giving 3-(arylmethyl)indoles.[12] After struggling to clarify the reaction mechanism of this skeletal remodeling process, we elucidated that the sp^2 carbon at the C3 position of the quinoline is reduced to the sp^3 carbon and rearranged to the benzylic position of the indole product. Interested readers might find it stimulating to consider how this skeletal editing reaction proceeds. This unexpected discovery has sparked a new research project in my laboratory. I hope to introduce it in the near future.

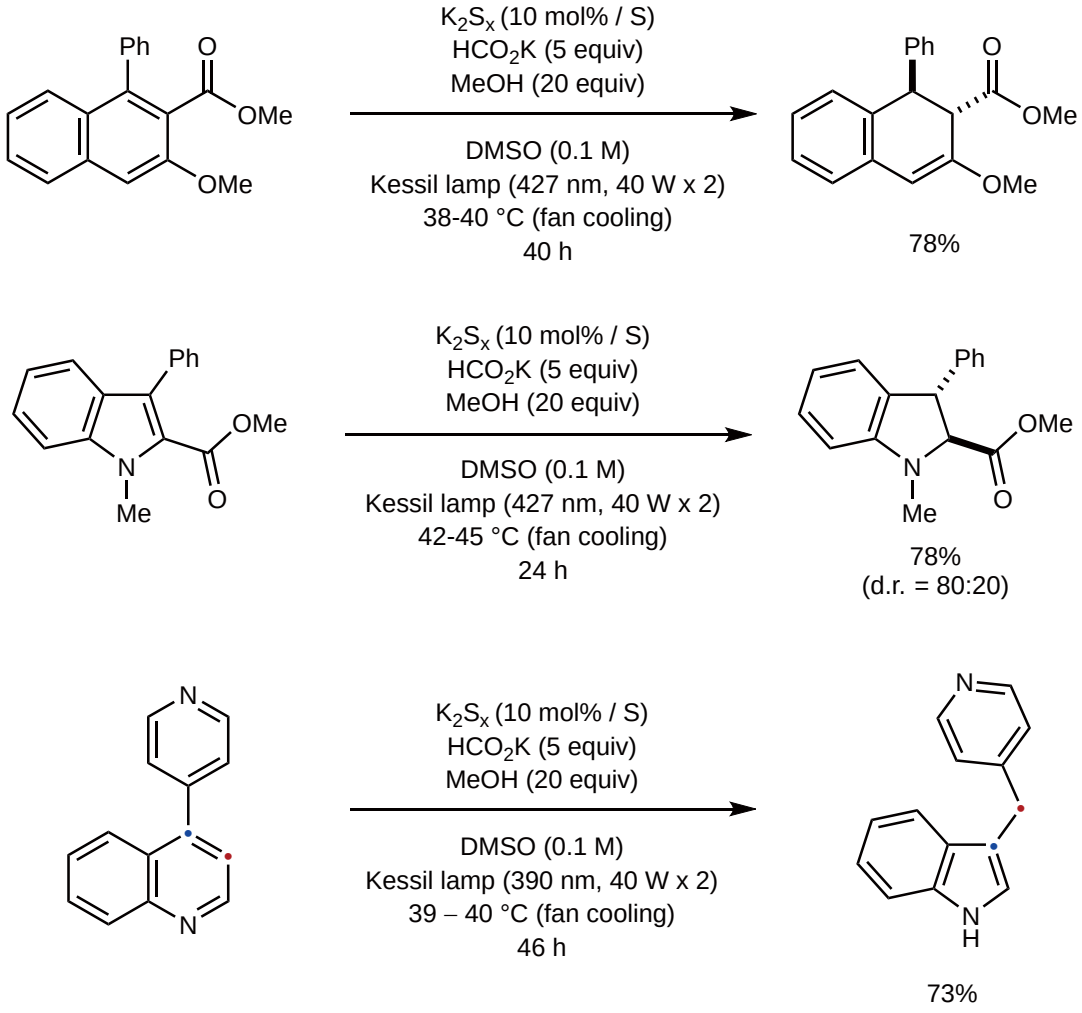


Figure 13

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2007 Tenure Track Assistant Professor, NTU Singapore
2012 Associate Professor with Tenure, NTU Singapore
2016 Professor of Chemistry, NTU Singapore

Related Products

Perylene Orange	1g	5g	B4268
Rhodamine 6G		25g	R0039
9,10-Dicyanoanthracene	1g	5g	D1656
Potassium Carbonate		300g	P1748
Potassium Formate	25g	500g	P3246

New Products Information

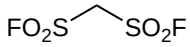
Sulfonyl Fluoride Derivative for SuFEx Reactions

Methanedisulfonyl Difluoride (1)

Product Number: **M4103**
1g 5g

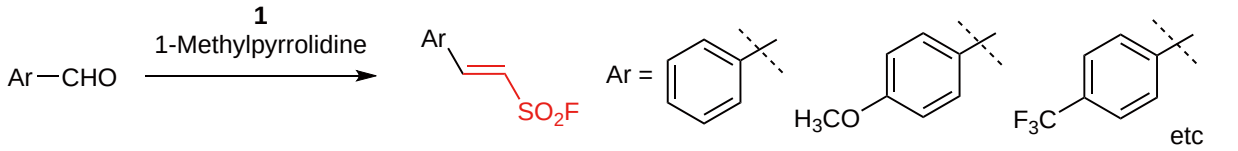
The SuFEx (sulfur fluoride exchange) reaction of nucleophiles such as amines and alcohols with compounds containing a sulfonyl fluoride group is utilized in various applications in various fields like drug discovery, chemical biology, and materials science. In drug discovery research, compounds with sulfonyl fluoride groups have been developed to react with target proteins.[1)]

Methanedisulfonyl difluoride (**1**) is a reagent used to introduce the sulfonyl fluoride moiety. For example, **1** can easily react with aromatic aldehydes to give α,β-unsaturated sulfonyl fluorides.[2)] In addition, when reacted with substituted α,β-unsaturated aldehydes, unique products such as α,β,γ,δ-unsaturated-α,α-disulfonyl difluorides can be obtained. The resulting unsaturated sulfonyl fluorides can be utilized in SuFEx reactions.

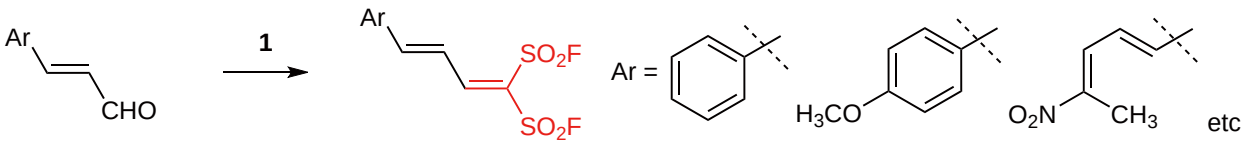


(**1**) **[M4103]**

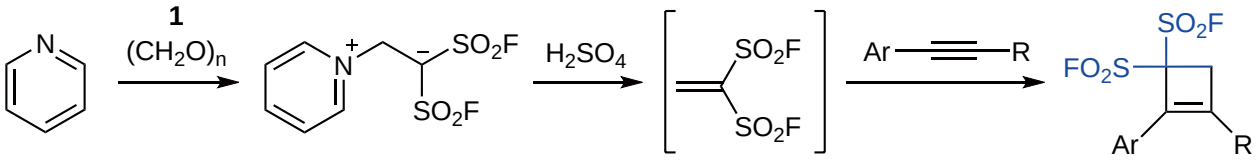
Horner–Wadsworth–Emmons type olefination



Knoevenagel type condensation



1,1-Disulfonyldifluoride ethene precursor (**EDSF-Precursor**, **2**), obtained from **1**, pyridine and paraformaldehyde, can be stored stably as an alternative to unstable EDSF. EDSF generated *in situ* from **2** undergoes [2+2] cycloaddition with alkynes to yield cyclobutene derivatives with two sulfonyl fluoride groups.[3)]



EDSF-Precursor (2)

Ethene-1,1-disulfonyl difluoride (EDSF)

References

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Related Product

Ethenesulfonyl Fluoride 1g V0143

Polylactic Acids: Biodegradable Polymers Contributing to the SDGs

Poly(L-lactic acid) (Mw=*ca*. 100000, ester terminated) (1) Product Number: **P3401** **5g 25g**

Poly(L-lactic acid) (Mw=*ca*. 200000, ester terminated) (2) Product Number: **P3402** **5g 25g**

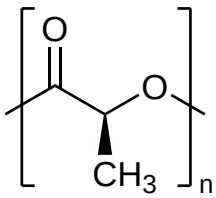
Poly(L-lactic acid) (Mw=*ca*. 300000, ester terminated) (3) Product Number: **P3403** **5g 25g**

Poly(DL-lactic acid) (Mw=*ca*. 100000, ester terminated) (4) Product Number: **P3398** **5g 25g**

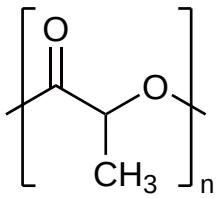
Poly(DL-lactic acid) (Mw=*ca*. 200000, ester terminated) (5) Product Number: **P3399** **5g 25g**

Poly(DL-lactic acid) (Mw=*ca*. 300000, ester terminated) (6) Product Number: **P3400** **5g 25g**

To address environmental pollution and climate change caused by petroleum-derived plastic waste, there is a growing demand to shift from a linear plastic economy, in which products are ultimately discarded, toward a sustainable circular economy.[1] Polylactic acid (PLA) is a biodegradable polyester typically synthesized from lactide derived from renewable resources such as corn. Because PLA ultimately degrades into water and carbon dioxide in biological environments and soil, it has attracted considerable attention as a green plastic.[2,3] Owing to these properties, PLA has found wide applications not only as a material for packaging containers and agricultural mulch films but also in the life science field, including biomedical components and drug delivery systems that take advantage of its biocompatibility. We offer a lineup of six PLA products including L- and DL-forms with average molecular weights of approximately 100000, 200000, and 300000 (**1**, **2**, **3**, **4**, **5**, **6**).
(These products are for research purposes only.)



(**1**) **[P3401]**
(**2**) **[P3402]**
(**3**) **[P3403]**



(**4**) **[P3398]**
(**5**) **[P3399]**
(**6**) **[P3400]**

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Acrylic Monomers Useful for Post-Polymerization Modifications

_N_-Succinimidyl Acrylate (1) — Product Number: **S0814** — **5g 25g**

_N_-Succinimidyl Methacrylate (2) — Product Number: **S0812** — **5g 25g**

_N_-Phthalimidyl Acrylate (3) — Product Number: **P3351** — **1g 5g**

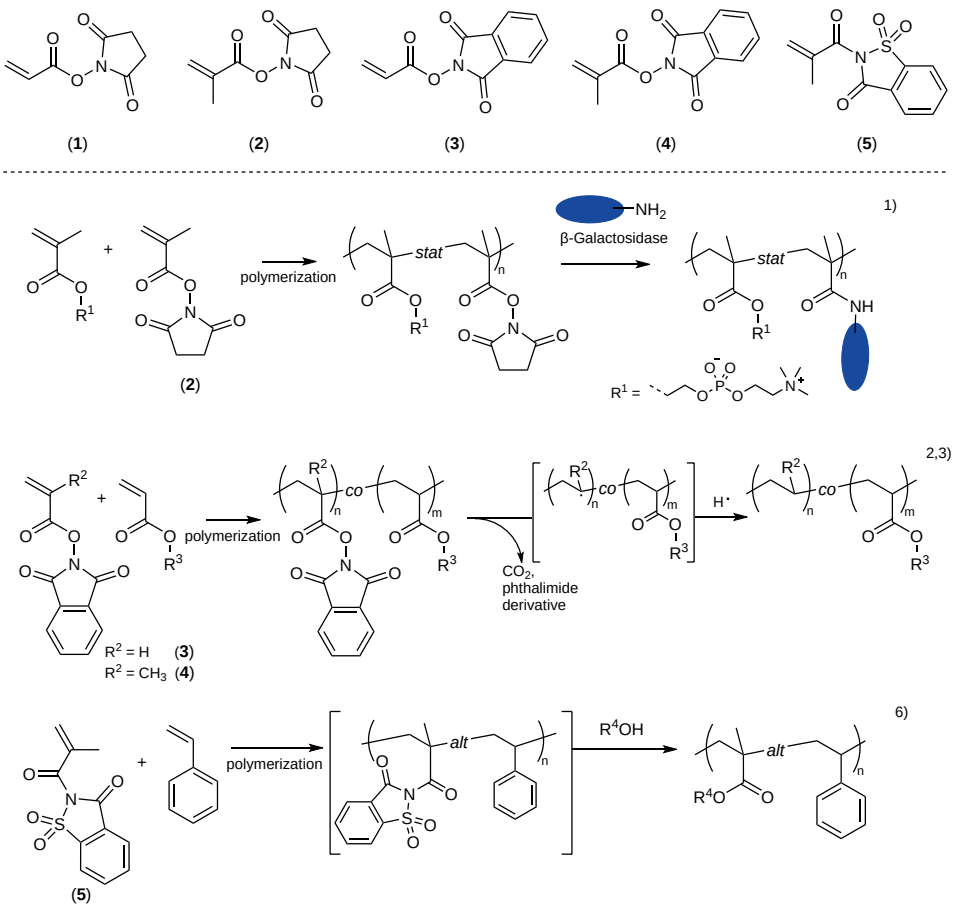
_N_-Phthalimidyl Methacrylate (4) — Product Number: **P3350** — **1g 5g**

Saccharin Methacrylamide (5) — Product Number: **A3463** — **1g 5g**

Post-polymerization modifications enable the synthesis of polymers with architectures that are difficult to obtain directly by polymerization and are therefore expected to be applied to the development of functional polymers. For instance, *N*-succinimidyl acrylate (**1**) and *N*-succinimidyl methacrylate (**2**), bearing a succinimide group, react with primary amines to form amide bonds. Therefore, these monomers have been used for the synthesis of polymers capable of immobilizing biomolecules such as enzymes.[1)]

Polymers derived from *N*-phthalimidyl acrylate (**3**) and *N*-phthalimidyl methacrylate (**4**), which contain a phthalimide group, can generate carbon radicals on the polymer backbone.[2,3)] Subsequent transformations via these radical intermediates, such as hydrogenation,[2,3)] alkene addition,[4)] and phosphonylation,[5)] have been reported. In the case of hydrogenation, the polymer units derived from **3** and **4** are converted into ethylene or propylene units, respectively.

Furthermore, saccharin methacrylamide (**5**) has been reported to yield alternating copolymers with styrene or conjugated dienes.[6,7)] The saccharin units in the copolymers are converted into alkyl methacrylate units through alcoholysis.



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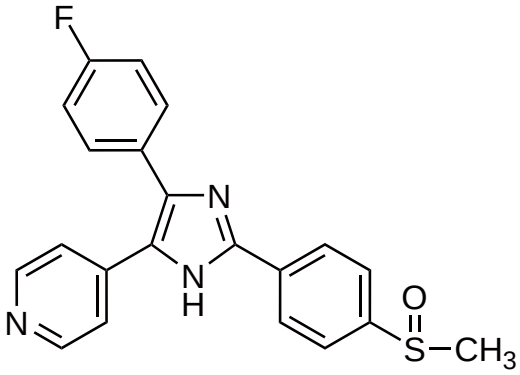
MAPK (Mitogen-activated Protein Kinase) Inhibitor

SB 203580 (1)

Product Number: **F0864**
25 mg 100 mg



(1)
[F0864]

SB 203580 (**1**) is a p38 MAPK inhibitor with IC_{50} values of 50 nM and 500 nM for SAPK2a/p38 and SAPK2b/p38β2, respectively.[1)] The inhibition mechanism of **1** to p38 MAPK is ATP competitive.[2)]

It has also been reported that inhibition of p38 by **1** allows the derivation of *Alk3* (*Bmpr1a*)$^{-/-}$ ES cell lines.[3)]
(This product is for research purposes only.)

Bmpr1a: bone morphogenetic protein receptor type 1a

References

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Related Product

SB 203580 [Optimized for Cell Culture]	1mg	B6670

L-Lactate Assay Kit for Cell Culture Supernatants and intracellular

L-Lactate Assay Kit (1)

Product Number: **L0507**
1kit

Glycolysis is a major metabolic pathway for producing energy, in which glucose is broken down in the cytosol to produce L-lactate.[1] Compared with normal cells, glycolytic activity has been reported to be increased in cancer cells.[2] As the main metabolic product of glycolysis, L-lactate is considered an important indicator of the cellular metabolic state. Consequently, quantifying L-lactate concentration is a common method used to evaluate alterations to metabolic pathways in cancer research and related fields.[3]

1 enables simple quantification of L-lactate in both cell culture supernatants and intracellular samples. A standard curve is generated using the supplied L-lactate standard solution, enabling L-lactate concentrations in samples to be calculated. **1** can measure concentrations from 0.02 to 1 mM; samples with concentrations exceeding 1 mM can be measured after appropriate dilution. This assay quantifies L-lactate concentration based on the absorbance change (at 450 nm) in the WST-8 reduction reaction catalyzed by NADH generated via the L-lactate dehydrogenase reaction (**Figure A**). Using **1** to evaluate cellular metabolic status, inhibition of glucose uptake by phloretin treatment resulted in a decrease in extracellular L-lactate concentration (**Figure B**). Conversely, inhibiting mitochondrial electron transport chain complex I with rotenone led to an increase in extracellular L-lactate concentration (**Figure B**). These results demonstrate that **1** is useful for evaluating changes in L-lactate concentration that reflect alterations in glycolytic activity and L-lactate transport.

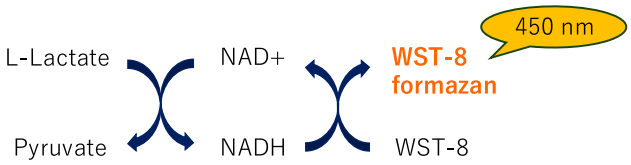

Figure A. Measurement principle of **1**.

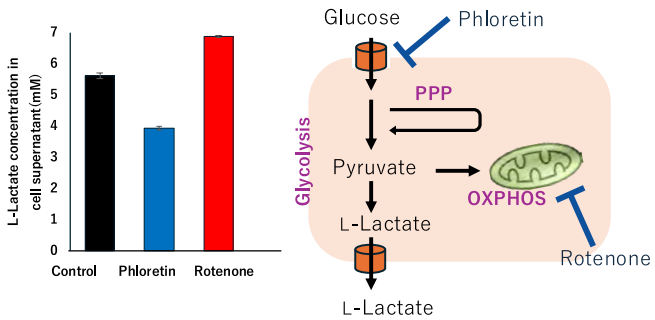

Figure B. L-Lactate concentrations in cell culture supernatants after treatment with phloretin and rotenone.

Experimental conditions
Cells: HeLa cells (5.0×10^4 cells)
Drug treatment duration: 24 h
Drug concentrations: phloretin, 100 µM; rotenone, 25 µM

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Related Products

Glucose Measurement Kit			1kit	G0656
2-NBDG			2mg	N1178
JC-1 Mitochondrial Membrane Potential Assay Kit			1kit	J0043
JC-1			50mg	T4300
Tetramethylrhodamine Methyl Ester Perchlorate		10mg	50mg	T3608
Intracellular Reactive Oxygen Species (ROS) Detection Assay Kit			1kit	I1265
Phloretin		1g	5g	P1966
Rotenone		5g	25g	R0090
2-Deoxy-D-glucose	1g	5g	25g	D0051
α-CHCA			1g	C1768

Highly Purified "Chondroitin Sulfate Proteoglycan" from Salmon Nasal Cartilage

Proteoglycan from Salmon nasal cartilage (1)

Product Number: **P3423**
10 mg

Proteoglycans are glycoproteins (glycoconjugates) in which high molecular weight polysaccharides (glycosaminoglycans: GAGs) are covalently attached to a core protein. They function as extracellular matrix components that exhibit diverse biological roles outside of cells. Proteoglycans derived from salmon nasal cartilage (**1**) mainly consist of GAG chains with structural diversity, in which several hydroxyl groups are sulfated in a linear repeating disaccharide backbone composed of glucuronic acid (GlcA) and *N*-acetylglucosamine (GlcNAc), known as chondroitin sulfate. In recent years, this material has attracted considerable attention as a func tional food ingredient, since animal studies have demonstrated cartilage tissue regeneration and confirmed improvements of joint function in human clinical trials.[1)]

1 is produced with rigorous quality control of proteoglycan purity through qualitative and quantitative analysis of unsaturated disaccharide structures obtained by the enzymatic digestion of chondroitin sulfate. **1** is suitable for applications such as quality evaluation of functional foods and research on the extracellular matrix.[2)] In addition, **1** is more affordable than conventional proteoglycan reagents.

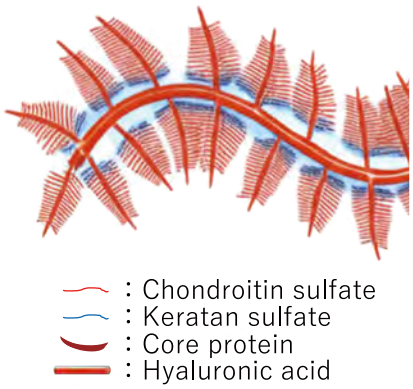

Figure. A conceptual illustration showing proteoglycan structure within cartilage tissue

1 has been commercialized under the technical tie-up with Nihon Pharmaceutical Co., Ltd. and Dr. Toshihiko Toida (Professor Emeritus, Chiba University).

References

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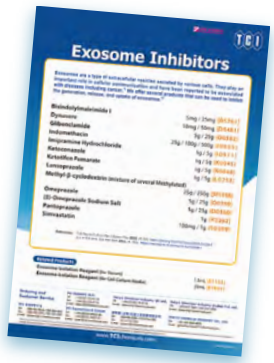

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