

Academic Program [Oral B] | 15. Organic Chemistry -Aliphatic and Alicyclic Compounds, and New Synthetic Technology- : Oral B

🏠 Thu. Mar 27, 2025 1:00 PM - 3:20 PM JST | Thu. Mar 27, 2025 4:00 AM - 6:20 AM UTC 🏠

[F]2401(2401, Bldg. 2, Area 4 [4F])

[[F]2401-2pm] 15. Organic Chemistry -Aliphatic and Alicyclic Compounds, and New Synthetic Technology-

Chair: Takuya Kochi, Kohei Takahashi

📌 English

1:00 PM - 1:20 PM JST | 4:00 AM - 4:20 AM UTC

[[F]2401-2pm-01]

Mechanochemical activation of metallic lithium enabling rapid generation of organolithium species and their applications to organic synthesis

○Keisuke Kondo¹, Koji Kubota^{1,2}, Hajime Ito^{1,2} (1. Graduate School of Engineering, Hokkaido University, 2. WPI-ICReDD, Hokkaido University)

📌 English

1:20 PM - 1:40 PM JST | 4:20 AM - 4:40 AM UTC

[[F]2401-2pm-02]

Catalytic Continuous-Flow Synthesis of Cyclic Carbonates using Gaseous and Supercritical CO₂

○ZHIBO YU¹, Haruro Ishitani¹, Shū Kobayashi¹ (1. the University of Tokyo)

📌 English

1:40 PM - 2:00 PM JST | 4:40 AM - 5:00 AM UTC

[[F]2401-2pm-03]

Continuous-Flow Aldol Condensation of Phenylacetate Derivatives with Formalin for α-Aryl Acrylate Synthesis

○Masahiro Sasaya¹, Haruro Ishitani¹, Shū Kobayashi¹ (1. The Univ. of Tokyo)

2:00 PM - 2:20 PM JST | 5:00 AM - 5:20 AM UTC

Break

📌 Japanese

2:20 PM - 2:40 PM JST | 5:20 AM - 5:40 AM UTC

[[F]2401-2pm-04]

Kinetic Analysis of Rapid Anionic Polymerization Using Quenched-Flow Method and Synthesis of Sequence-Controlled Copolymers

Shuto Oshida¹, ○Hiromichi V. Miyagishi¹, Hodaka Sakaue¹, Aiichiro Nagaki¹ (1. Department of Chemistry, Faculty of Science, Hokkaido University)

📌 English

2:40 PM - 3:00 PM JST | 5:40 AM - 6:00 AM UTC

[[F]2401-2pm-05]

N- and P-Doped Carbon-Supported Platinum Catalysts for Selective Reductive Coupling of Nitro Compounds with Aldehydes to Nitrones

○Taisei Senzaki¹, Tomohiro Yasukawa^{1,2}, Shu Kobayashi¹ (1. The University of Tokyo, 2. Monash University)

📌 Japanese

3:00 PM - 3:20 PM JST | 6:00 AM - 6:20 AM UTC

[[F]2401-2pm-06]

Hydrogenation of Alkenes Using Atmospheric-Pressure Nonthermal Plasma

○Takaya Fujie^{1,3}, Yoichi Kitazawa¹, Takuya Kochi¹, Tomohiro Nozaki^{2,3}, Fumitoshi Kakiuchi^{1,3} (1. Keio University, 2. Institute of Science Tokyo, 3. JST-CREST)

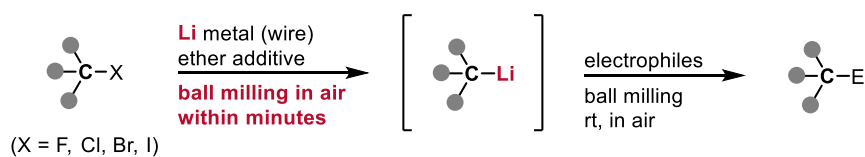
Mechanochemical activation of metallic lithium enabling rapid generation of organolithium species and their applications to organic synthesis

(¹Graduate School of Engineering, Hokkaido University, ²WPI-ICReDD, Hokkaido University)
 ○Keisuke Kondo,¹ Koji Kubota,^{1,2} Hajime Ito^{1,2}

Keywords: Mechanochemistry; Ball mill; Organolithium species; Lithium; Metalation

Mechanochemical synthesis, which uses ball-milling to induce chemical reactions, has garnered increased interest in various fields of organic chemistry in recent years.¹ In the area of organometallic synthesis, this method can eliminate the need for complicated operational setups involving inert gases and dry organic solvents and enhance reactivity by activating the surface of zero-valent metals.² However, the mechanochemical generation of organolithium compounds has not yet been explored systematically despite the widespread use of such compounds as arguably one of the most fundamental and valuable organometallic reagents in organic synthesis.

Here, we report the first mechanochemical protocol for the direct generation of organolithium reagents from readily available organic halides and unactivated lithium source (lithium wire) under bulk-solvent-free conditions.³ These reactions rapidly (within minutes) generate a diverse array of organolithium compounds at room temperature without special precautions against moisture and temperature control, and the addition of these compounds to various electrophiles proceeds smoothly in a one-pot fashion. Moreover, the solid-state ball-milling conditions enable the generation of organolithium reagents from poorly soluble aryl halides, which are incompatible with conventional solution-based conditions. Furthermore, the present mechanochemical strategy allows the rapid and direct generation of organolithiums via C–F bond lithiation without using pre-activated lithium sources. Given these attractive features, the present study constitutes an important milestone in the field of organometallic mechanochemistry.



- ▶ Carried out under ambient conditions ▶ Bulk-solvent-free conditions ▶ Fast metalation (within minutes)
- ▶ Applicable to poorly soluble substrates ▶ No requirement for activated Li sources

- 1) J. Reynes, F. Lenon, F. García, *Acs Org. Inorg. Au*, **2024**, 4, 432.
- 2) (a) R. Takahashi, A. Hu, P. Gao, Y. Gao, Y. Pang, T. Seo, S. Maeda, J. Jiang, H. Takaya, K. Kubota, H. Ito, *Nat. Commun.* **2021**, 12, 6691. (b) P. Gao, J. Jiang, S. Maeda, K. Kubota, H. Ito, *Angew. Chem. Int. Ed.* **2022**, 61, e202207118.
- 3) K. Kondo, K. Kubota, H. Ito, *Nat. Synth.* *accepted*.

Catalytic Continuous-flow Cyclic Carbonate Synthesis with Gaseous and Supercritical CO₂

(¹ Department of Chemistry, School of Science, The Univ. of Tokyo, ² GSC Social Cooperation Laboratory, Graduate School of Science, The Univ. of Tokyo)

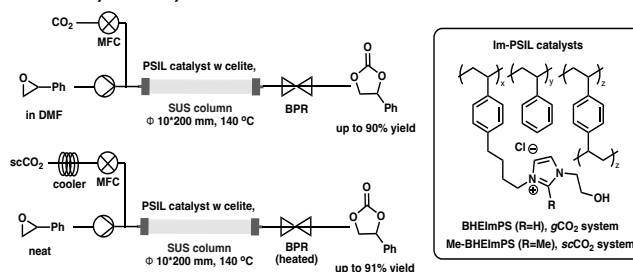
○Zhibo YU,¹ Haruro ISHITANI,² Shū KOBAYASHI^{1, 2}

Keywords: Polymer-supported Catalyst; Ionic Liquid; CO₂; Cyclic Carbonate; Continuous-flow Reaction

CO₂, a common waste gas massively emitted in industrial and agricultural production as well as daily activity, is on the other hand counted as the most ideal and valuable C1 source for the production of organic chemicals as well. Recently, Carbon Capture and Utilization (CCU), as a significant strategy with large-scale emission reduction potential to achieve the goal of carbon neutrality, has been developed worldwide. Notably, supercritical CO₂ (scCO₂) exhibits characteristics which make it widely utilized in organic synthesis, especially CO₂ conversions where it can function as both reactant and solvent. As well as nontoxicity and incombustibility, both its high thermal conductivity enabling systems free from the interference from reaction heat and the powerful capability on mass transfer ascribed to its low viscosity in porous solid catalysts consequently make it surpass conventional organic solvents.^{1,2} As one of well-developed applications, the synthesis of cyclic carbonates from epoxides has drawn increasing interest due to their promising industrial uses, such as aprotic polar solvents, benign intermediates for polymer synthesis, etc. In view of high energy barriers of the reaction between CO₂ and epoxides, efficient catalyst design allowing the activation of cycloaddition is the essence of the work. Polymer-supported ionic liquids (PSILs), with exceptional chemical stability, designability and unique catalytic ability, have been testified efficient on cyclic carbonate synthesis by facilitating both the capture and activation of epoxides, and synergistical ring-opening process.

In this study, we utilized a series of PSIL catalysts in a continuous-flow cyclization of epoxides with CO₂. We synthesized variously substituted imidazolium polymers using polystyrene with a 4-bromobutyl linker. Among them, resins bearing hydroxyethyl group proved to be beneficial for the reaction to attain high yields. Based on those findings, we further modified the structure to obtain the optimal catalysts, guaranteeing continuous 90% and 91% yields under gaseous and supercritical CO₂ conditions. In the presentation, we will discuss the latest progress of this research project.

Continuous-flow Synthesis of Cyclic Carbonate:



1) Baiker, A. *Chem. Rev.*, **1999**, 99, 453-474.

2) Baiker, A. *et al.*, *Catal. Rev.* **2003**, 45, 1-96.

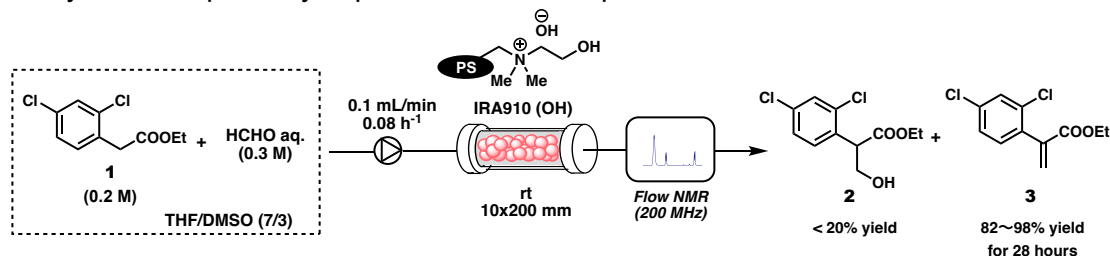
Continuous-Flow Aldol Condensation of Phenylacetate Derivatives with Formalin for α -Aryl Acrylate Synthesis

(School of Science¹ and GSC Social Cooperation Laboratory,² The Univ. of Tokyo)

○ Masahiro SASAYA,¹ Haruro ISHITANI,² Shū KOBAYASHI^{1, 2}

Keywords: Continuous-flow Reaction; Aldol Condensation; Heterogeneous Catalyst; Anion Exchange Resin; Quaternary Ammonium Hydroxide Resins

α -Aryl acrylic acid derivatives are important intermediates in the synthesis of polymers and fine chemicals. Their synthesis from the ester and formaldehyde have relied on the catalytic gas-phase reactions or the use of a stoichiometric amount of base,^{1,2} and thus condensation under liquid-phase is a desired method for realizing low-energy processes. While it was known that the use of a catalytic amount of base afforded β -hydroxy ester,³ a continuous-flow system with a catalyst-packed bed reactor will change its reaction outcome to acrylates thanks to the high density of catalyst packed to substrate than the batch system. Through investigations of the reaction conditions, we succeeded in drawing out an efficient catalysis of quaternary ammonium hydroxide resin for the reaction of phenylacetate derivatives **1** with formalin, especially when using DMSO solvent, but at the same time, saponification of the ester proceeded as a side reaction. We then optimized the cation structure and searched for a suitable resin that would effectively catalyze the reaction with suppressing the saponification. As a result, dimethylethanolammonium resin was found to be the optimal for the selective production of the desired acrylate **3** under flow conditions. When this catalyst system was applied for the extended-time reaction, the desired acrylate was obtained with a ratio of 80/20 or more for 28 h under SV = 0.08 h⁻¹. Further extension of the flow operation resulted in lowering the ratio while maintaining the total yield of the condensation products. This change in selectivity was suggested to be related to the total amount of water supplied and produced by the reaction. In addition, a detailed comparison of the reaction kinetic profiles of the batch and the flow system suggested that under the optimal flow conditions, the stepwise mechanism was dominant for the outcome, but that there existed a mechanism for direct formation of acrylate via a pathway separate from the stepwise reaction.



- 1) Z. Li, *et al.*, *Chemical Engineering Science* **2022**, 247, 117052.
- 2) Y. Zhang, *et al.*, *Org. Lett.* **2021**, 23, 21, 8359–8364.
- 3) Z. X. Jiang, Z. Yang, *et al.*, *Org. Biomol. Chem.*, **2016**, 14, 7463–7467.

クエンチフロー法による高速アニオン重合の反応速度解析と配列制御共重合体の合成

(北大院理¹) 押田 秀斗¹・○宮岸 拓路¹・阪上 穂高¹・永木 愛一郎¹

Kinetic Analysis of Rapid Anionic Polymerization Using Quenched-Flow Method and Synthesis of Sequence-Controlled Copolymers (¹*Department of Chemistry, Faculty of Science, Hokkaido University*) Shuto Oshida,¹ ○Hiromichi V. Miyagishi,¹ Hodaka Sakaue,¹ Aiichiro Nagaki¹

Copolymers, synthesized from diverse types of monomers, offer a wide range of functionalities as polymer materials. The properties of these copolymers are strongly influenced by the sequence of monomers and their molecular weight distribution. While sequential monomer addition is commonly used to control monomer sequences, rapid copolymerization reactions, such as anionic polymerization, remain difficult to analyze and control due to the extended mixing times in conventional batch reactors.¹ In this study, we successfully analyzed the kinetics of fast anionic polymerization reactions using a flow microreactor, which enables rapid mixing and precise control of reaction time. Furthermore, we synthesized sequence-controlled copolymers through the instant addition of monomers and evaluated the effects of monomer sequences on the physical properties of the copolymers.

Keywords : *Living anionic polymerization; Kinetic analysis; Flow microreactor*

複数のモノマーから合成される共重合体は多様な機能を有することが知られており、その物性は共重合体中のモノマー配列や分子量分布に大きく影響を受ける。こうした共重合体の配列制御手法としては、反応速度解析に基づいた逐次的なモノマー追添加などが広く知られている。しかしながら、従来のバッチ型反応器を用いた手法は基質の混合時間が遅いため、アニオン重合をはじめとする高速な共重合反応の解析・制御は困難であった¹。本研究では、高速な混合および精密な滞留時間制御が可能なフローマイクロリアクター(FMR)を活用してスチレンの重合反応を瞬間的に停止させることで、数秒以内で完結する高速なアニオン重合の反応速度解析を達成した。また、FMR を用いてモノマー追添加と反応停止を瞬時に行うことで配列制御共重合体を合成することにも成功し、モノマー配列が高分子物性に与える影響を評価した。

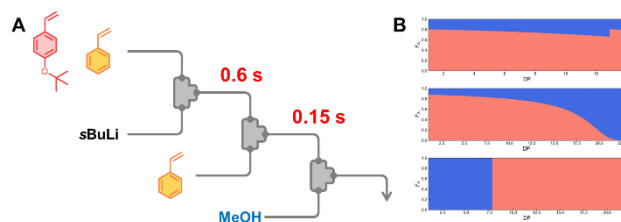


Fig. (A) モノマー追添加条件での配列制御共重合体の合成と、(B)得られた共重合体のモノマー組成

1) Reaction rate analysis of styrene anionic polymerization using the quench-flow method has been reported. Geacintov, C.; Smid, J.; Szwarc, M. *J. Am. Chem. Soc.* **1962**, *84*, 2508–2514.

N- and P-Doped Carbon-Supported Platinum Catalysts for Selective Reductive Coupling of Nitro Compounds with Aldehydes to Nitrones

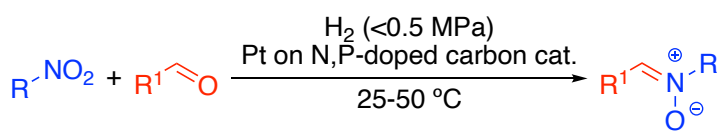
(School of Science, The Univ. of Tokyo¹ • Monash Univ.²) ○Taisei SENZAKI,¹ Tomohiro YASUKAWA,^{1,2} Shū KOBAYASHI¹

Keywords: Heterogeneous Platinum Catalyst; N- and P-doped Carbon Support; Selective Hydrogenation Reaction; Nitron; Continuous-flow Reaction

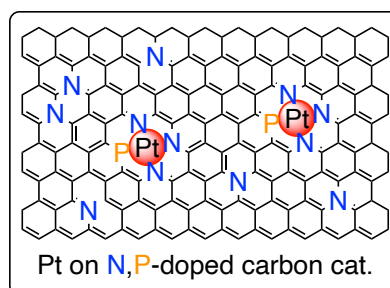
Single-atom catalysts (SACs) are easily separable and recyclable heterogeneous catalysts with well-defined active centers.¹⁾ SACs incorporate the advantages of both homogeneous and heterogeneous systems, enabling sustainable and efficient reactions. SACs-catalyzed hydrogenations are known to proceed via an unconventional mechanism; a hydrogen molecule is activated by heterolytic dissociation at single-atomic sites, as opposed to homolytic activation by nanoparticle species.¹⁾ Nevertheless, studies that exploit the unique features of SACs for selective hydrogenation reactions remain scarce.

The reductive coupling of nitro compounds and aldehydes using hydrogen gas and heterogeneous catalysts is an environmentally friendly synthetic method for nitrones, with water as the only byproduct.²⁾ However, control of side-reductions poses a significant challenge. Therefore, we hypothesized that the selectivity could be manipulated by fine-tuning of the catalyst structure, such as coordination sites.

We prepared nitrogen- and phosphorus-doped carbon-supported platinum catalysts as SACs based on a recent report.³⁾ The platinum catalysts showed remarkable selectivity in the target coupling reactions over commercial platinum nanoparticle catalysts. Possible side-reactions such as hydrogenation of nitron products, hydroxylamine intermediates to primary amines, and aldehydes to alcohols were suppressed. In addition, phosphorus dopants on the carbon support enhanced the catalytic activity for the conversion of nitro compounds compared to nitrogen-doped carbon-supported catalysts. As a result, the desired nitrones were afforded in high yields and selectivity. Moreover, the method was applicable to a wide range of substrates and continuous-flow reactions, which have never been achieved before. Further details will be discussed in the presentation.



batch high yields, >40 examples
flow >80% yield (0-24 h), R = Ph, R' = 2-furyl



- 1) Huang, Y.; Zhou, W.; Zhang, B. *et al. J. Mater. Chem. A* **2022**, 10, 5743.
- 2) Serna, P.; Corma, A. *et al. Angew. Chem. Int. Ed.* **2014**, 53, 9306.
- 3) Yasukawa, T.; Kobayashi, S. *et al. J. Am. Chem. Soc.* **2023**, 145, 11939.

大気圧非熱プラズマを利用したアルケンの水素化反応

(慶大理工¹・科学大工²・JST-CREST³) ○藤江 峻也^{1,3}・北澤 瑤一¹・河内 卓彌¹・野崎 智洋^{2,3}・垣内 史敏^{1,3}

Hydrogenation of Alkenes Using Atmospheric-Pressure Nonthermal Plasma

(¹*Faculty of Science and Technology, Keio University*, ²*Graduate School of Engineering, Institute of Science Tokyo*, ³*JST-CREST*) ○Takaya Fujie,^{1,3} Yoichi Kitazawa,¹ Takuya Kochi,¹ Tomoyuki Nozaki,^{2,3} Fumitoshi Kakiuchi^{1,3}

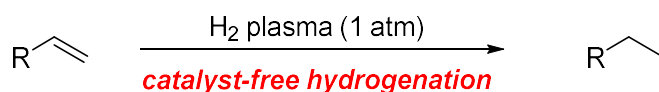
Atmospheric-pressure nonthermal plasma, which is in a nonequilibrium state where only electrons are at much higher temperature than other species in a gas phase, has attracted much attention as a unique source of reactive chemical species at low temperature. However, there have been a limited number of studies of organic reactions using this technology, because of the lack of availability of the special equipment that enables the application of the nonthermal plasma to standard organic reaction systems.¹

Here we report on the development of the batch reaction systems applicable to laboratory-scale reactions using organic solutions with a flow of non-thermal atmospheric pressure plasma generated by dielectric barrier discharge. Using this apparatus, hydrogenation of alkenes was found to proceed in the absence of any catalysts.

Keywords : *Hydrogenation of Alkenes; Nonequilibrium Plasma; Radical Reaction; Hydrogen Radical; Catalyst-Free Hydrogenation*

大気圧非熱プラズマは、イオンを含めた気相中の様々な化学種に対して電子のみがより高温であるという非平衡状態にあることから、プラズマ中の活性種を低温で利用できる手段として注目され、多くの研究がなされてきた。しかし、このプラズマを通常の有機反応装置において簡便に利用可能な手段がないことから、有機合成化学の分野への応用例はいまだ限られている。¹

今回我々は、通常の実験室内で用いるガラス容器内において、大気圧下での誘電体バリア放電により非熱プラズマを発生させ、有機溶媒中での有機小分子との反応を遂行可能な装置を開発した。また、この装置を用いて、プラズマ化した水素ガスを有機溶媒中でアルケンと反応させたところ、無触媒での水素化が進行したので報告する。



1) (a) Gorbanev, Y.; Leifert, D.; Studer, A.; O'Connell, D.; Chechik, V. *Chem. Commun.* **2017**, 53, 3685–3688. (b) Xu, X.; Zhao, X.; Tang, J.; Duan, Y.; Tian, Y. *Angew. Chem. Int. Ed.* **2022**, 61, e202203680. (c) Wang, J.; Üner, N. B.; Dubowsky, S. E.; Confer, M. P.; Bhargava, R.; Sun, Y.; Zhou, Y.; Sankaran, R. M.; Moore, J. S. *J. Am. Chem. Soc.* **2023**, 145, 10470–10474.