

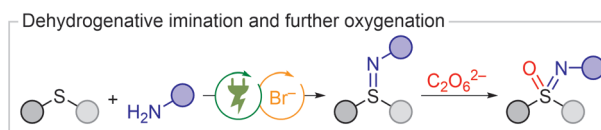
# Synform

People, Trends and Views in Chemical Synthesis

2023/08

## Dehydrogenative Imination of Low-Valent Sulfur Compounds – Fast and Scalable Synthesis of Sulfilimines, Sulfinamidines, and Sulfinimidate Esters

Highlighted article by M. Klein, D. L. Troglauer,  
S. R. Waldvogel



### Contact

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please correspond if you like:  
[marketing@thieme-chemistry.com](mailto:marketing@thieme-chemistry.com)

## Dear Readers,

Last week – after all the media hype and having attended a lecture on the topic by an expert here at the European Commission in Brussels - I tried ChatGPT for the very first time. I instructed it to write a brief text – about half an A4 page – on several general topics, from the sea of Sardinia to novel trends in organic chemistry. The latter, obviously hoping the AI tool would write SYNFORM editorials for me?... Well, unfortunately the brief texts were okay – I cannot say it was rubbish – the content was there, but the style was super flat, no personal touch or any sign of irony – as you would expect from ChatGPT. I even tried to feed it with 5 of my previous editorials to see whether it could somehow mimic my style and come up with a livelier text, but I still could not see much improvement. No hope to use it for writing my editorials, for now at least... Frankly, for the time being I do not see how someone could let ChatGPT do the job for him/her and get away with that, unless this person is very poor at writing, of course... But I suspect that in six or twelve months ChatGPT & Co will be able to do a much better job, and at some point – in the not-too-distant future – SYNFORM could be efficiently run by an AI algorithm without any need for a human editor. I am absolutely convinced it will happen and probably nobody will miss me or any other human editor. I just hope I will be retired on a beach, enjoying a cocktail, when this happens... but will this be the case of the next generations too? Will their jobs be taken by AI? Will we all get a salary just to watch the AI do our jobs? Will we eventually end up in a Matrix-style world? There are so many opportunities, but also challenges and worrying aspects in the not-so-virtual world of AI...

But for today let's focus on a rock-solid and far-from-artificial August issue of SYNFORM. It kicks off with the novel, efficient and scalable synthesis of sulfilimines, sulfinamidines, and sulfinimidate esters developed and published in *JACS Au* by the group of S. R. Waldvogel

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(Germany), and remains in the same country with the exciting *Science* paper on enantioselective electrochemical cobalt-catalyzed aryl C–H activation reactions from the group of L. Ackermann. With the next Literature Coverage article, we move to the Republic of Korea where the group of D.-P. Kim has recently published in *Nat. Commun.* a brand-new method to generate the trifluoromethyl anion from gaseous  $\text{CF}_3\text{H}$  in flow via rapid biphasic mixing, leading to a range of trifluoromethylated compounds. Last, but not least, there is a Young Career Focus interview with 2023 Thieme Chemistry Journals Awardee C. Zhu (P. R. of China).

Enjoy your reading!

*Matteo Zanda*

### Contact

If you have any questions or wish to send feedback, please write to Matteo Zanda at: [synform@outlook.com](mailto:synform@outlook.com)

# Dehydrogenative Imination of Low-Valent Sulfur Compounds – Fast and Scalable Synthesis of Sulfilimines, Sulfinamidines, and Sulfinimide Esters

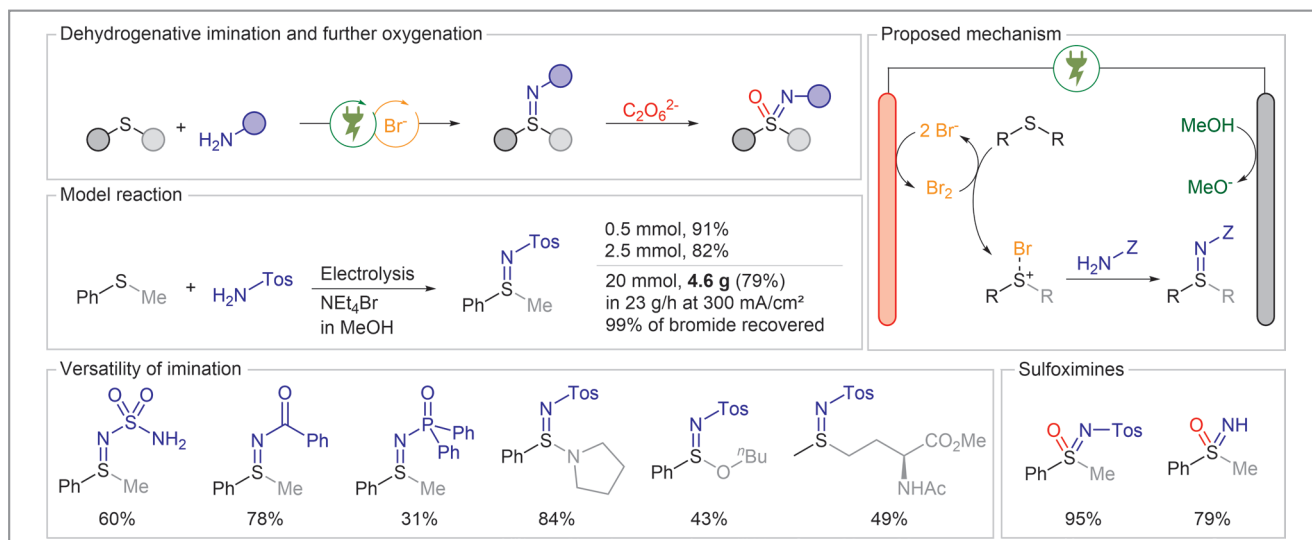
*JACS Au* **2023**, *3*, 575–583

Sulfur-containing functional groups are of utmost importance in medicinal chemistry. This is due to their structural diversity as well as their frequent natural occurrence. The pharmaceutical landscape of trivalent sulfur species is dominated by sulfoxides, sulfinates, and sulfinamides. The use of other potential candidates in drug discovery, such as sulfilimines, sulfinimide esters, and sulfinamidines, is an underexplored topic. This is mainly due to the lack of protocols for the preparation of these classes of compounds, which are often converted into their corresponding tetravalent siblings – such as sulfoximines – which are of high value for medicinal chemistry applications.

The Waldvogel research group at the Johannes Gutenberg University Mainz (Germany) has extensive expertise in electro-organic transformations. Professor Waldvogel explained: “This technique is often regarded as one of the most promising 21<sup>st</sup> century methods for avoiding the use of hazardous and waste-producing oxidants or reducing agents. Consequently, it is experiencing a renaissance in academic and technical synthesis. The use of low-cost electric power is a sustainable force to gently drive redox reactions.” He continued: “The importance of specialized sulfur-based functional

groups, together with the expertise in electro-organic transformations, led us to investigate new methods for preparing these valuable compounds.”

In the literature, halide-assisted oxidation of thioethers in the presence of strong bases is described as a general approach for this transformation. To avoid the handling of these toxic and corrosive reagents, the group investigated halide-mediated electrochemical oxidation using easy-to-handle and common salts. “This can be combined with the formation of electrochemically generated bases at the cathode,” said Professor Waldvogel. He continued: “We investigated this hypothesis using thioanisole and *p*-toluenesulfonamide as test substrates. Indeed, selective formation of the sulfilimine was observed when bromide was used as the mediator and MeOH as the base. In addition, bromide and MeOH also served as supporting electrolyte and solvent, which allowed for an extremely efficient use of the reactants.” The group used a modern Design of Experiments (DoE)-based optimization strategy to increase the product yield and to study the critical parameters of this transformation. This allowed a rapid evaluation of the process and resulted in a product yield of 91%. “We adapted the method slightly to make it applicable



**Scheme 1** Summary of results for the dehydrogenative imination of low-valent sulfur compounds

to less stabilized sulfilimines, such as the benzamide-derived substrates, which gave only moderate yields with the previous method,” remarked Professor Waldvogel, who went on: “Using these two approaches, we were able to synthesize a variety of different sulfilimines, sulfinamides, and sulfinamidate esters. Numerous amides as well as various low-valent sulfur compounds were converted into the corresponding sulfur-nitrogen compounds. We were able to show that the developed method has a high robustness. It can be operated at many current densities from 1 to 1000 mA/cm<sup>2</sup>. It can be scaled to several grams with very short reaction times, which represents a powerful method for technical development. A transfer of the reaction to a flow cell has also been successful.”

In further studies, the group investigated the reaction mechanism and were able to prove that their hypotheses were correct. The bromide was oxidized at the anode, forming an electrophilic bromonium species that reacts with the starting materials. Depending on the nature of the nucleophile, it reacts with either the sulfur compound or the amide. Both lead to the formation of the desired compound, but with different by-products.

Professor Waldvogel said: “Finally, we wanted to develop a new method to convert the formed sulfilimines into highly pharmaceutically relevant sulfoximines. Since no overoxidation was observed during electrolysis, we focused on the use of electrochemically generated oxidants in this project. The use of peroxodicarbonate, prepared by oxidation of carbonate stock solutions on boron-doped diamond (BDD) electrodes, allowed very selective oxidation with excellent yields. Acetonitrile plays a crucial role in this process for efficient oxygen transfer.”

Professor Waldvogel concluded: “In summary, the group has developed a new protocol for the electrochemical synthesis of several trivalent sulfur-nitrogen compounds such as sulfilimines, sulfinamidines, and sulfinimidate esters. These were converted into highly valuable sulfoximines using a carbonate-mediated system. A modular process for the preparation of such pharmaceutically relevant compounds is described. The mediator for imination can be recovered quantitatively by aqueous extraction. Combined with the high robustness of the method, this leads to a high potential for use as a sustainable technical synthesis. Electrochemistry is becoming an increasingly powerful technique in organic synthesis. Its application, with few exceptions, is limited to small-scale synthesis in academia. General approaches to transfer these methods to large-scale industrial production and to electrify technical organic synthesis need to be explored to unlock the great potential of this sustainable method.”

*Mattias Fenske*

### About the authors



Dr. M. Klein

**Martin Klein** studied biomedical chemistry in Mainz, Germany. He received his BSc at the Johannes Gutenberg University (Germany) in 2017 and his MSc in the group of Prof. Waldvogel in 2019, focusing on electrochemical hydrogenations. He did his PhD in the field of electro-organic synthesis until 2023 and is currently working as a postdoc at the Merck group in Darmstadt (Germany) on sustainable synthesis in process development.



D. Troglauer

**David Troglauer** received his BSc under the supervision of Prof. Waldvogel at Johannes Gutenberg University (Germany) in 2021 where he focused on the electrochemical synthesis of *N*-sulfilimines. In 2022, he joined the group of Prof. Streb to continue his graduate studies.



Prof. S. Waldvogel

**Siegfried R. Waldvogel** studied chemistry in Konstanz (Germany) and received his PhD in 1996 from University of Bochum/Max Planck Institute for Coal Research (Germany) with Prof. M. T. Reetz. After postdoctoral research in La Jolla, CA (USA) with Prof. J. Rebeck, Jr., he started his own research at the Universities of Münster and Bonn (Germany). He became full professor at JGU Mainz (Germany) in 2010.

His research interests are novel electro-organic transformations including bio-based feedstocks. In 2018, he cofounded ESy-Labs GmbH, which provides custom electrosynthesis and contract R&D.

## Enantioselective Electrochemical Cobalt-Catalyzed Aryl C–H Activation Reactions

*Science* **2023**, *379*, 1036–1042

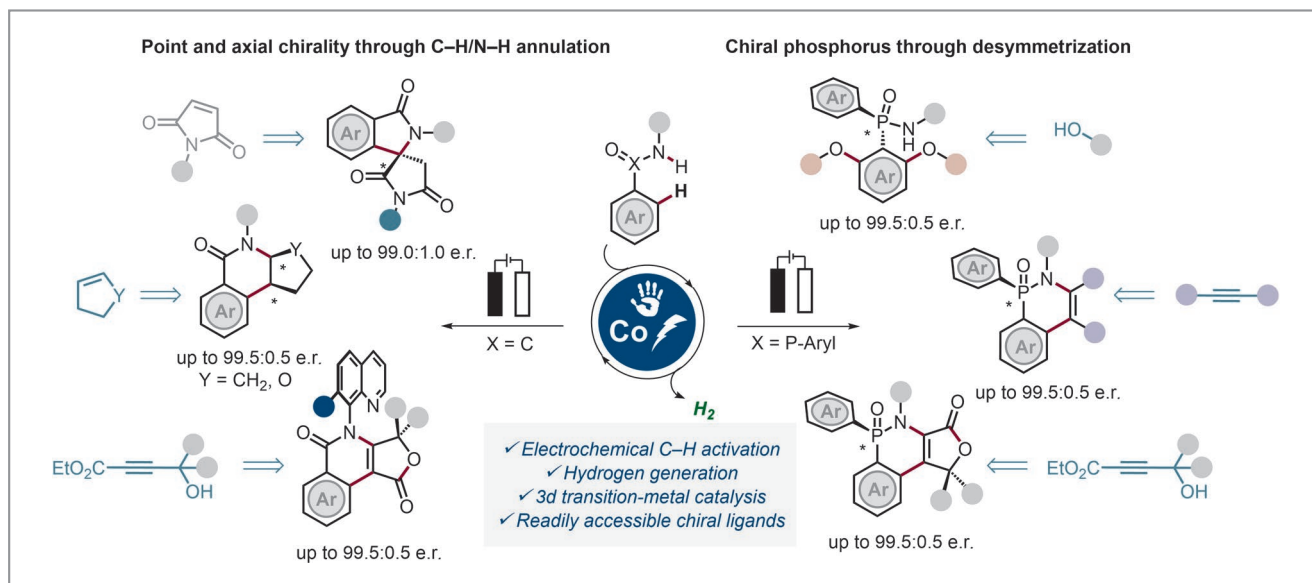
The three-dimensional absolute configuration of an organic molecule plays a critical role in defining its physical and biological activity. Hence, the stereoselective synthesis of organic compounds is of exceptional importance, especially in the fields of flavours and fragrances, in agrochemistry, as well as in drug development. In this regard, enantioselective catalysis has proven to be a powerful tool and continuous efforts have been devoted to design novel asymmetric transformations and apply them for practical usage. “Here, transition-metal-catalyzed C–H activation reactions remained at the forefront, owing to their sustainable nature and broad utility prospects,” said Professor Lutz Ackermann, from the Georg-August-Universität Göttingen (Germany); “However, a large majority of these transformations make use of expensive and toxic 4d transition metals in combination with sophisticated chiral ligands, which constitutes a considerable limitation.” Professor Ackermann’s research group recently developed a novel approach to this issue, which was published in the title article. “When evaluating an enantioselective catalysis in the context of green chemistry, we should not overlook the resource and financial effort that goes into the synthesis of the chiral ligand,” first author Tristan von Münchow explained. “Furthermore, super-stoichiometric amounts of transition-metal-based oxidants are commonly employed to accomplish the redox manipulation of the transition-metal catalyst during these transformations, which leads to the formation of hazardous waste, representing substantial sustainability issues.” In this context, Prof. Ackermann emphasized that the use of super-stoichiometric amounts of transition-metal silver salts is a major challenge for an industrial scale, adding: “It is worth noting that trace metal impurities are strictly controlled in pharmaceutical products.”

Professor Lutz Ackermann’s research group has been continuously devoting significant attention to addressing these key challenges of enantioselective transition-metal-catalyzed C–H activation reactions. “In previous years, specific focus has been paid to develop metalla-electrocatalyzed approaches, where the stoichiometric waste generation from the additives can be avoided using the hydrogen evolution reaction (HER) to enable anodic oxidations as a sustainable means to manipulate the oxidation states of the transition-metal catalysts,” explained Professor Ackermann. “This electro-oxidative

approach has been successfully employed to develop first examples of enantioselective C–H activations with palladium and rhodium catalysis (*Chem. Sci.* **2022**, *13*, 2783–2788; *Chem. Sci.* **2022**, *13*, 2729–2734; *Chem. Sci.* **2021**, *12*, 14182–14188; *Angew. Chem. Int. Ed.* **2020**, *59*, 13451–13457).” He continued: “In order to further realize the sustainability aspects of catalytic enantioselective C–H activation, the use of 3d transition metals as catalysts is an important research topic of our group. Pioneering work has been done in this area in the recent past.” Thus, the first enantioselective iron-catalyzed C–H activation was developed in 2017 (*Angew. Chem. Int. Ed.* **2017**, *56*, 14197–14201) and the first high-valent enantioselective cobalt(III)-catalyzed C–H activations in the following year (*Angew. Chem. Int. Ed.* **2018**, *57*, 15425–15429; proof of concept: *Angew. Chem. Int. Ed.* **2017**, *56*, 10378–10382). However, the latter are redox-neutral transformations, and the Ackermann group is now focusing on enantioselective redox transformations by means of sustainable 3d transition-metal electrocatalysis. “In our recent venture we have reported the first example of electrooxidative cobalt-catalyzed enantioselective C–H activations, where easily accessible chiral phosphoric acid and salicyloxazoline (Salox) ligands are used to induce enantioselectivity,” said Professor Ackermann.

“We have described six enantioselective transformations to demonstrate the diverse potential of enantioselective cobalt-electrocatalysis (Scheme 1),” explained Professor Ackermann. He continued: “The transformations include the synthesis of chiral spirolactams incorporating a quaternary stereogenic center, enantio- and diastereoselective carboamination of olefins, and the synthesis of axially stereogenic molecules through C–H/N–H annulation reactions. The desymmetrization of phosphinic amides has also been achieved to construct chiral P-centered molecules. These strategies avoid the use of stoichiometric oxidants and harvest electricity in a dual role as sacrificial oxidant and for multi-site concerted proton-electron transfer (CPET) to generate hydrogen gas as the only by-product through cathodic proton reduction, which makes this strategy useful to construct a decentralized green hydrogen economy.”

Interestingly, the spirocyclization of benzamides with maleimides was achieved using simple and commercially available unsubstituted BINOL phosphoric acid as the chiral



**Scheme 1** Schematic representation of enantioselective electrochemical cobalt-catalyzed C-H activation reactions

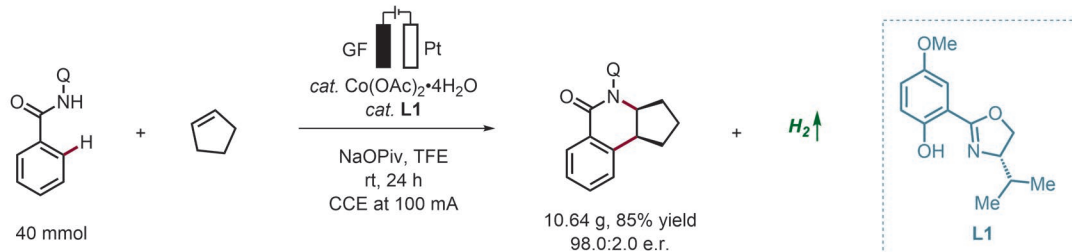
ligand, while other substituted chiral phosphoric acids were found to be ineffective. “This trend of reactivity with simple chiral phosphoric acid disclosed the unique nature of electrochemical organic synthesis,” remarked Professor Ackermann, who went on: “Mechanistic studies revealed that the reaction rate is controlled by the electron transfer and spectro-electrochemical studies supported a viable Co(III)/Co(IV)/Co(II) pathway by means of oxidation-induced reductive elimination (see also: *Angew. Chem. Int. Ed.* **2020**, *59*, 10955–10960).”

The diastereoselective carboamination, atroposelective synthesis of C–N axially chiral molecules, and desymmetrization of phosphinic amides were achieved using chiral Salox ligands, derived from commercially available 1,2-amino alcohols. All these transformations are operationally simple, offer high enantioselectivity, and endure various common functionalities on the arenes. Professor Ackermann said: “The reactions are scalable and the enantioselective carboamination reaction was performed even on a decagram scale (Scheme 2). Though the developed methods generally use Pt-cathodes due to its low overpotential for HER, the scalable transformation can also be performed using inexpensive stainless steel as the cathode material, showing their synthetic usability. These transformations also tolerate fluctuating current and voltage, which is demonstrated by executing the desymmetrization of phosphinic amides using a commercial solar panel. Here, the electrooxidation is directly achieved converting natural solar energy to electrical energy, which is then translated into chemical bonds.”

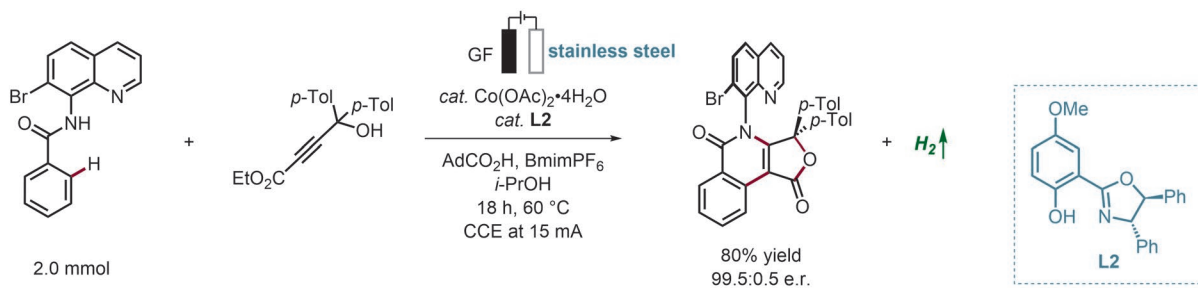
“We have disclosed a versatile resource-economic electro-oxidative cobalt catalysis, which is applicable for the synthesis of various chiral organic molecules with high selectivity control,” explained Professor Ackermann. He continued: “The ease of scalability without affecting the reaction outcome and the direct use of solar energy to perform the catalysis along with cathodic HER demonstrate the exceptionally robust features of these transformations, which can be easily translated for other sustainable enantioselective syntheses using 3d transition metals.” He concluded: “We are very happy to observe that our findings on robust metalla-electrocatalysis have rapidly inspired numerous scientists around the globe to advance science towards a sustainable future (for example: *Angew. Chem. Int. Ed.* **2023**, e202302964; *Green Chem.* **2023**, *25*, 3606–3614).”

*Matteo Farab*

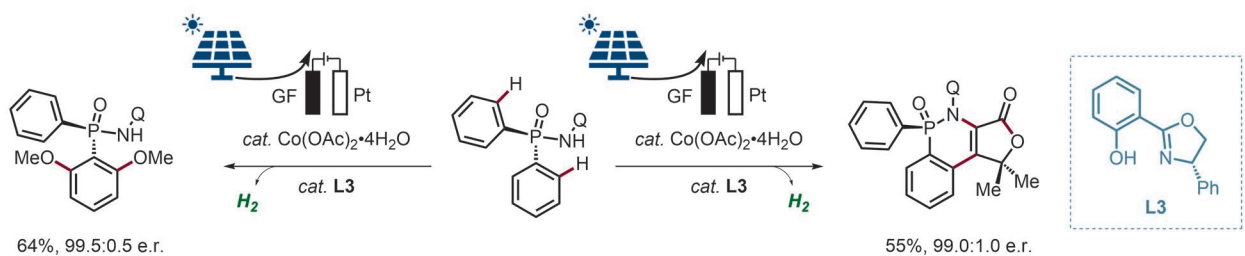
• Enantio- and Diastereoselective C–H/N–H Annulation on Decagram Scale:



• Scalable Atroposelective C–H/N–H Annulation Using Stainless Steel Cathode:



• Asymmetric Desymmetrization of Phosphinic Amides Harvesting Solar Energy:



Scheme 2 Synthetic applicability of enantioselective electrochemical cobalt catalysis

## About the authors



T. von Münchow

**Tristan von Münchow** was born in 1996, in Bayreuth, Germany. He received his B.Sc. in chemical and environmental engineering from TH Lübeck, Germany, and M.Sc. in chemistry from Georg-August-Universität Göttingen, Germany. Since 2021 he has been a Ph.D. student at the same university under the supervision of Prof. Lutz Ackermann. In 2022, he received the Kekulé Fellowship from the Fonds der Chemischen Industrie. His

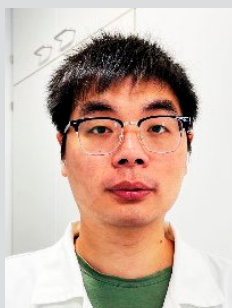
research interest is the enantioselective catalytic C–H bond activation through Earth-abundant 3d transition metals.



Dr. S. Dana

**Suman Dana** was born in 1992, in West Bengal, India. He earned his bachelor's degree in chemistry (honours) from Bankura Christian College, India, and master's degree (gold medallist) from School of Chemistry, University of Hyderabad (India). He received his Ph.D. in April 2021 from the Indian Institute of Technology, Madras (India) under Dr. Mahiuddin Baidya's supervision. In 2021, he joined the research group

of Prof. Lutz Ackermann at the Georg-August-Universität Göttingen (Germany) as a postdoctoral researcher, where he is involved in developing new asymmetric transformations using metalla-electrocatalyzed C–H bond activation reactions.



Y. Xu

**Yang Xu** was born in 1992, in Henan province, China. In July 2016, he earned his bachelor's degree in chemistry from Yan'an University, China, and his master's degree in July 2019 from Zhengzhou University, China. He then worked as a mid-level researcher at Viva Biotech Ltd (Shang Hai) and as a research assistant at Shenzhen Bay Laboratory from 2019 to 2022. In 2022, he joined the research group

of Prof. Lutz Ackermann at the Georg-August-Universität Göttingen (Germany) as a Ph.D. student. His research interest is the enantioselective catalytic C–H bond activation through Earth-abundant 3d transition metals.



B. Yuan

**Binbin Yuan** was born in 1993, in Hebei province, China. She received her bachelor's degree in the School of Chemistry and Chemical Engineering of Lanzhou University, China, and Master's degree in physical chemistry from Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences (China). She is now pursuing her Ph.D. under the supervision of Prof. Lutz Ackermann at the

Georg-August-Universität Göttingen (Germany). Her current research interests focus on computational mechanistic studies of transition-metal-catalyzed C–H transformations.



Prof. L. Ackermann

**Lutz Ackermann** studied chemistry at the University Kiel (Germany) and performed his Ph.D. with Prof. Alois Fürstner at the Max-Planck-Institut für Kohlenforschung (Mülheim/Ruhr, Germany, 2001). After a postdoctoral stay at UC Berkeley (USA) with Prof. Robert G. Bergman, he initiated his independent research career in 2003 at the Ludwig-Maximilians-Universität München (Germany). In 2007, he became a Full Professor (W3) at the

Georg-August-Universität Göttingen (Germany). His recent awards and distinctions include an AstraZeneca Excellence in Chemistry Award (2011), an ERC Consolidator Grant (2012), a Gottfried-Wilhelm-Leibniz-Preis (2017), and an ERC Advanced Grant (2021). The development and application of novel concepts for sustainable catalysis constitutes his major current research interests, with a topical focus on electrocatalysis and bond activation.

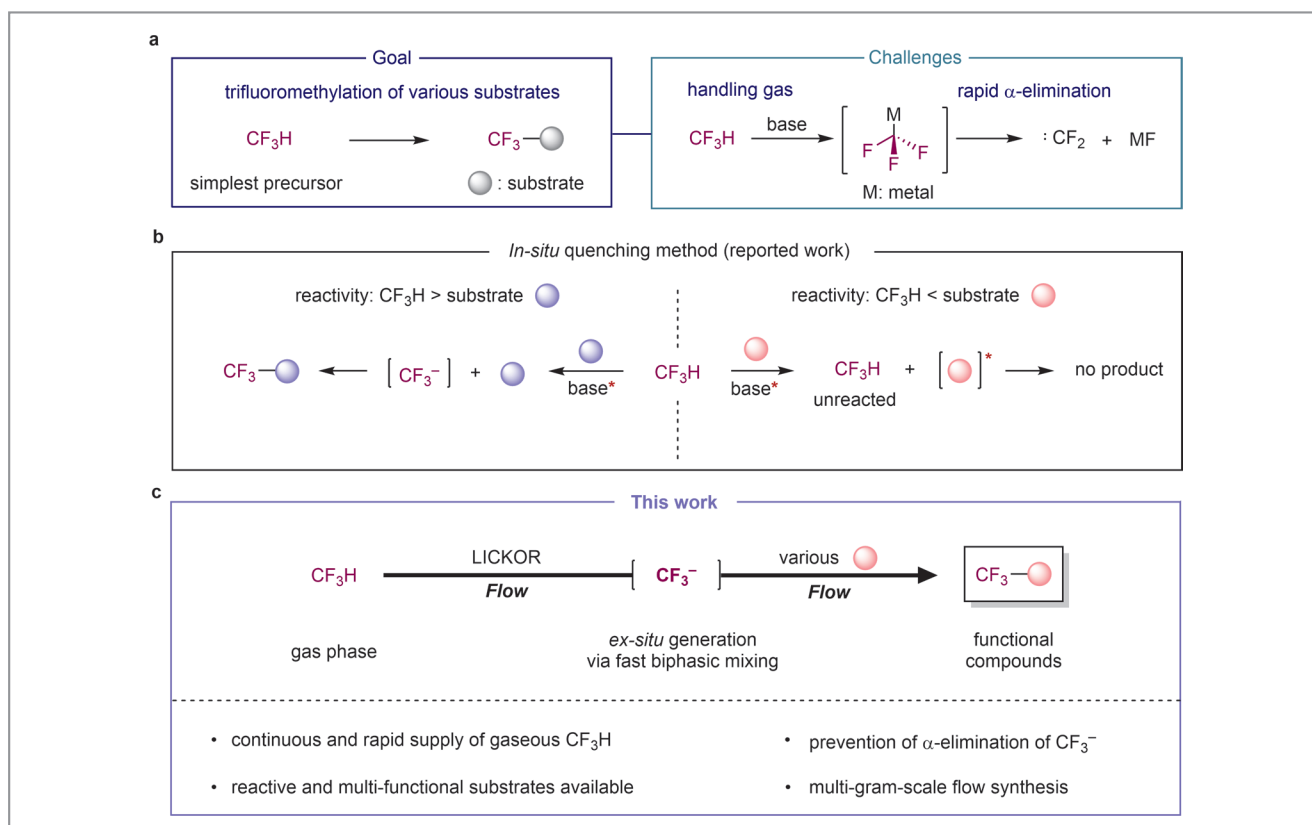


# Ex-Situ Generation and Synthetic Utilization of Bare Trifluoromethyl Anion in Flow via Rapid Biphasic Mixing

*Nat. Commun.* **2023**, *14*, 1231

The trifluoromethyl (CF<sub>3</sub>) group has been recognized as an important functional group in medicinal chemistry, because it can improve the therapeutic efficacy and metabolic stability of bioactive molecules. Additionally, it has been discovered that it can play a significant role in enhancing the binding affinity to intracellular proteins, which is crucial for the pharmacological efficacy of organic compounds. Therefore, the development of pharmaceuticals containing the trifluoromethyl functional group has been a booming research field, and according to the World Drug Index (WDI), fluorine-containing new drugs are leading the trend. Professor Dong-Pyo Kim at the Pohang University of Science and Technology (Republic of Korea) and co-workers have been working on novel approaches to CF<sub>3</sub>-containing molecules, which are exclusively man-made,

resulting in this paper in *Nature Communications*. Professor Kim said: "Among the extensive synthetic strategies for introducing the CF<sub>3</sub> group, various synthetic methodologies for nucleophilic trifluoromethylation have been developed, but there is no better way than to directly use fluorocarbon (CF<sub>3</sub>H) as the simplest precursor of the CF<sub>3</sub> group in the viewpoint of atom- and step-economy (Figure 1a). However, the synthetic utility of gaseous CF<sub>3</sub>H still remains limited because of its difficult handling and low reactivity." Above all, as remarked by Professor Kim, the reaction intermediate of the nucleophilic trifluoromethylation, the CF<sub>3</sub> anion (CF<sub>3</sub><sup>-</sup>), rapidly decomposes into difluorocarbene (:CF<sub>2</sub>) and fluoride anion. "To avoid these issues, many researchers have adopted the *in-situ* quenching method (Figure 1b), where the reaction substrate (or partner)



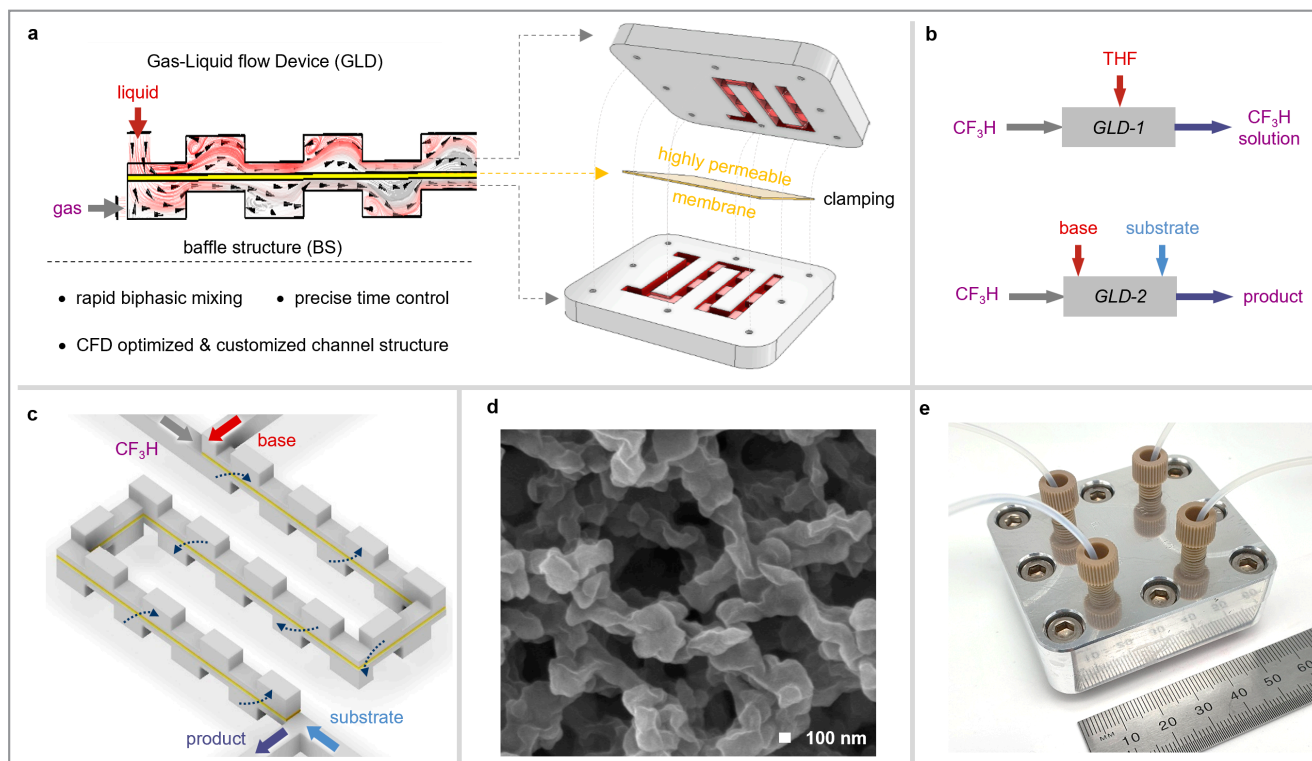
**Figure 1** Methods for nucleophilic trifluoromethylation using CF<sub>3</sub>H

coexists with  $\text{CF}_3^-$ ,” explained Professor Kim. He continued: “Nevertheless, this *in-situ* quenching requires additional reagents for the stabilization of  $\text{CF}_3^-$  and has fatal problems of narrowing down the reaction scope and selectivity when this reaction substrate is hardly compatible with the reaction conditions for generating the desired intermediate. To overcome the critical limitations of the *in-situ* quenching method and preserve the original strong reactivity of the unstable  $\text{CF}_3^-$ , the latter should be formed in the absence of any reaction partner or stabilizing reagent, prior to its subsequent reaction (i.e., *ex-situ* quenching method) (Figure 1).”

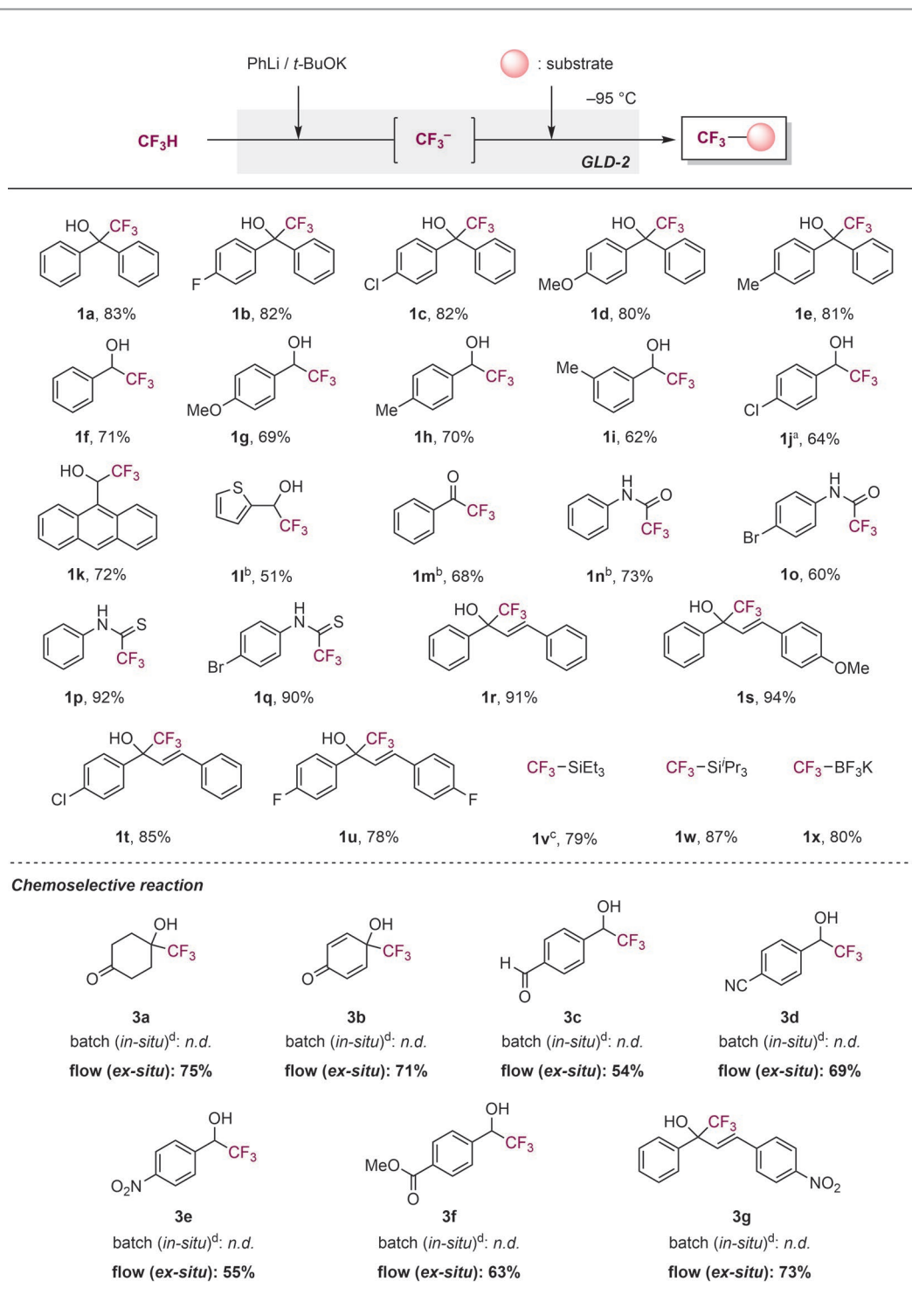
Professor Kim emphasized that despite the fact that the *ex-situ* quenching method is a powerful approach for synthesizing and utilizing  $\text{CF}_3^-$ , it has not been applicable to the generation of  $\text{CF}_3^-$  from  $\text{CF}_3\text{H}$ . This is because it is challenging to achieve both a fast biphasic mixing of gaseous  $\text{CF}_3\text{H}$  with liquid deprotonating reagent within the short lifetime of  $\text{CF}_3^-$  and a precise time-control for the external trapping reaction with generated  $\text{CF}_3^-$ , even using flow-type reactors that are well-known to afford rapid mixing efficacy unachievable in flask. “In this study, we designed and fabricated a specialized gas-liquid flow device (GLD) to address the long-standing problem in gas-liquid chemical processes,” said Professor Kim.

He continued: “Based on the fact that efficient biphasic mixing for rapid dissolution can be achieved by a large contact area between gas and liquid with a smaller size gas bubble, we conceptually designed flow channel structured dissolvers composed of highly permeable nano-porous membrane sandwiched between upper and lower channels with staggered baffle structure (Figure 2). The baffle structured channels induced chaotic advection involving rapid distortion of the fluid interface when the gas-liquid mixture flows over the upper and the lower channels, while the nano-porous membrane in the middle acted as a static mixer and bubble breaker by preventing coalescence of gas segments which must severely reduce the contact area. By developing this novel gas-liquid mixing reactor concept, we were able to efficiently generate the  $\text{CF}_3^-$  intermediate solely and subsequently introduce the reactant compound to perform the fluorination reaction.”

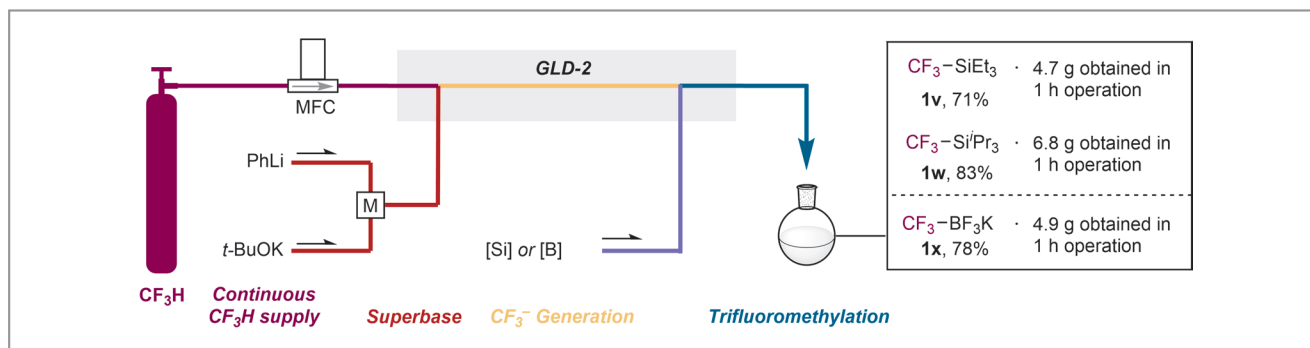
With this method, the researchers found that the reaction with various electrophilic substrates was successfully achieved in 51–94% yield, which is quite remarkable. Professor Kim remarked: “In particular, the powerful advantage of the *ex-situ* method was demonstrated by the chemoselective nucleophilic addition with substrates bearing two electron-withdrawing groups (Scheme 1). Additionally, the multi-gram



**Figure 2** Design and fabrication of gas-liquid flow device (GLD) including highly permeable membrane and staggered baffle channel



**Scheme 1** The reaction of bare  $\text{CF}_3^-$  with various electrophilic substrates in GLD-2. Isolated yields are given. <sup>a</sup> The resulting  $\text{CF}_3^-$  solution was allowed to react with an electrophile at  $-50\text{ }^\circ\text{C}$ . <sup>b</sup> The resulting  $\text{CF}_3^-$  solution was allowed to react with an electrophile at  $-78\text{ }^\circ\text{C}$ . <sup>c</sup> TESCI (2 equiv) was used. <sup>d</sup> The yield was determined by  $^1\text{H}$  NMR spectroscopy using an internal standard.



**Figure 3** The multi-gram-scale synthesis using an integrated flow system involving GLD-2

synthesis was successfully conducted within a 1-hour operation of our gas-liquid flow device to synthesize the three important chemical reagents which are used for nucleophilic trifluoromethylation (71–83%, 4.7–6.8 g/h) (Figure 3). The device enabled the one-flow  $\text{CF}_3\text{H}$  supply, the formation of superbases,  $\text{CF}_3^-$  generation, and trifluoromethylation. The method allows us not only to reveal accurate information on the lifetime and stability of  $\text{CF}_3^-$  but also to conduct the chemoselective reaction with various substrates, thus addressing a fundamental obstacle with the *in-situ* quenching method.”

“In summary, to the best of our knowledge, this is the first report involving the generation and utilization of  $\text{CF}_3^-$  from  $\text{CF}_3\text{H}$  via the *ex-situ* quenching method,” said Professor Kim, adding: “We expected that the well-established flow device would rationalize the *ex-situ* generation and utilization of  $\text{CF}_3^-$  from the rapid gas-liquid mixing between the strong base and  $\text{CF}_3\text{H}$  gas, the simplest trifluoromethylation resource. With this device, the *ex-situ* generation and utilization of  $\text{CF}_3^-$  was conducted within only 0.44 seconds even under highly cryogenic conditions, and various electrophiles were also reacted with  $\text{CF}_3^-$  anion in a much higher yield, compared to the *in-situ* method. Moreover, we successfully achieved the chemoselective reaction with multi-functionalized electrophiles, which were only successfully conducted by the *ex-situ* quenching method in the flow reaction.” Professor Kim concluded: “We believe that this approach provides an advanced reaction platform for the utilization of various unstable intermediates from the biphasic reaction.”

*Matthew Farah*

## About the authors



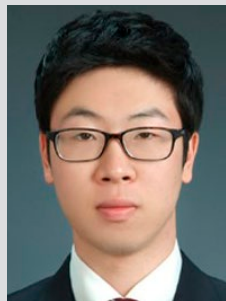
Prof. D. P. Kim

**Dong-Pyo Kim** graduated with a BSc in chemistry from Sogang University (Seoul) in 1985. Then he moved to the USA where he was awarded his PhD in 1991 from Temple University before becoming a postdoctoral researcher at the University of Illinois from 1991–1993. He then returned to Korea and took up a post as a senior researcher at the Korea Research Institute of Chemistry. In 1995 he moved on to a position as Professor of Applied Chemistry at Chungnam National University (Korea) and was promoted to head of the Center of Applied Microfluidic Chemistry in 2008. In 2012 he was also appointed as Professor of Chemical Engineering at the Pohang University of Science & Technology (Korea). In addition, in 2017 he became Head of the Center for Intelligent Microprocess of Pharmaceutical Synthesis and in 2022 he became the CTO of Flow-medi. He still holds the last three positions.



Prof. HJ Kim

**Heejin Kim** was a JSPS Research Fellow in 2010–2011 and spent the first six months of 2011 as a visiting Research Fellow at the Massachusetts Institute of Technology (USA). Following this, he returned to Korea and in lieu of military service spent two years (2011–2013) as a Research Fellow at the Korea Institute of Science and Technology (KIST) and a further two years at the Pohang University of Science and Technology (POSTECH) from 2013–2015. In 2015 he moved to Kyoto University (Japan) as a Research Assistant Professor. Later that same year, he moved back to Korea and took up a post as Assistant Professor at Korea University before being promoted to Associate Professor at the same university in 2020.



Dr. H. J. Lee

**Hyune-Jea Lee** completed his PhD at the Pohang University of Science and Technology (POSTECH, Korea) in 2019. He then spent six months as a postdoctoral researcher at the same university. In 2019, he moved to Korea University (Korea) for three years as a postdoctoral researcher. Then in 2022 he moved to the Samsung Advanced Institute of Technology (SAIT, Korea) as a researcher.



J. U. Joo

**Jeong-Un Joo** studied for his BSc from 2013–2019 at Ajou University (Korea). He is now a graduate student at the Pohang University of Science and Technology (POSTECH, Korea).



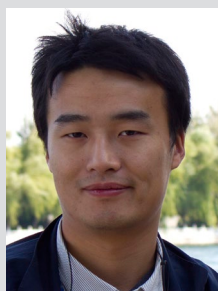
Dr. S. J. Yim

**Se-Jun Yim** obtained his BSc from Ajou University (Korea) in 2017. He then undertook his PhD at the Pohang University of Science and Technology (POSTECH, Korea) from 2017–2023. He is now a researcher at SK hynix (Korea).

## Young Career Focus: Dr. Can Zhu (Fudan University, P. R. of China)

**Background and Purpose.** SYNFORM regularly meets young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This Young Career Focus presents Dr. Can Zhu (Fudan University, P. R. of China).

### Biographical Sketch



Dr. C. Zhu

**Can Zhu** received his PhD under the supervision of Prof. Shengming Ma from Shanghai Institute of Organic Chemistry (SIOC), P. R. of China in 2014. After that, he started his postdoctoral studies in the group of Prof. Jan-E. Bäckvall at Stockholm University (Sweden). In September 2016, he was awarded an Alexander von Humboldt Foundation Postdoctoral Fellowship to join Prof. Frank Glorius's research group, Westfälische Wilhelms-Universität Münster (Germany), working on non-noble metal catalysis. In July 2018, he moved back to Stockholm University, and worked there as a researcher until joining Prof. Konrad Tiefenbacher's group at University of Basel (Switzerland). In November 2020, Can Zhu began his independent research career at Fudan University, Shanghai, P. R. of China. Currently, his research group's interests focus on the development of dynamic kinetic resolution (DKR) for the synthesis of chiral molecules from racemates. In 2023, he was the recipient of a Thieme Chemistry Journals Award.

### INTERVIEW

**SYNFORM** *What is the focus of your current research activity?*

**Dr. C. Zhu** The research interests of our group mainly focus on the synthesis of chiral molecules via dynamic kinetic resolution (DKR, Scheme 1 left) and dynamic kinetic asymmetric transformations (DYKAT, Scheme 1 right). Chirality has found wide applications in materials science and pesticide and drug development. The current methodologies mainly focus on the asymmetric addition of planar molecules (e.g. olefins, aldehydes, and ketones). Kinetic resolution of racemates is another important means to achieve chiral synthesis, but its yield is theoretically limited to 50%. Moreover, the reaction termination point is difficult to control, which often leads to low enantioselectivity of products. Dynamic kinetic resolution (DKR) can effectively overcome this problem (Scheme 1 left). In this field, the development of efficient, selective and compatible racemic catalysts is the key element to promote the development of DKR technology.

**SYNFORM** *When did you get interested in synthesis?*

**Dr. C. Zhu** I was introduced to organic chemistry when I was in college. At the beginning, I planned to engage in theoretical chemistry, but later in the experimental course, I discovered that synthetic chemistry was so amazing and attractive, and can create different compounds through different catalysts and reaction conditions, and even can create substances that were not originally in this world. Since then, I decided to pursue research in synthetic chemistry.

>>

**SYNFORM** Could you tell us something about yourself outside the lab, such as your hobbies or extra-work interests?

**Dr. C. Zhu** In addition to scientific research, our team have group activities every week, such as playing basketball, badminton, and watching movies together. Personally, I prefer sports, such as basketball. Doing exercise can keep people healthy, and offer a good platform to strengthen communication with team members.

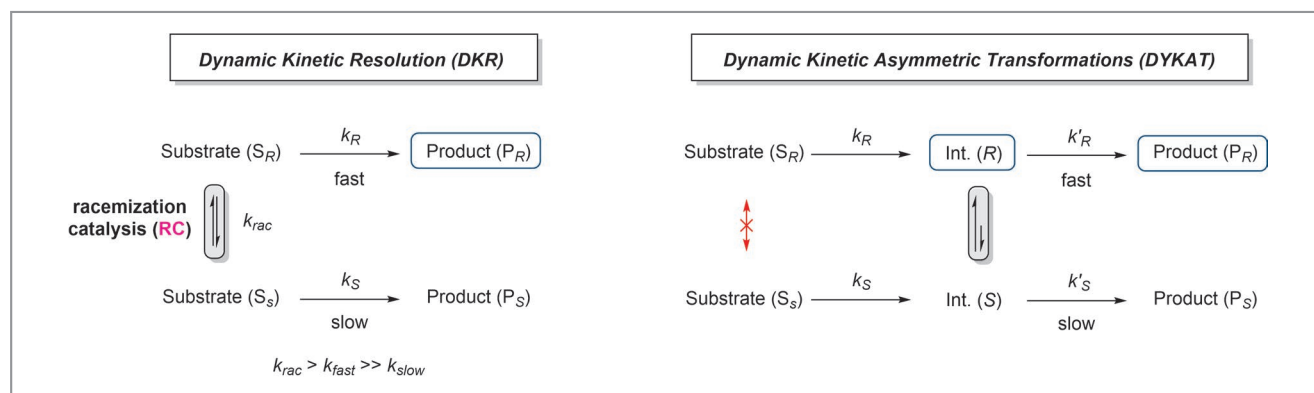
**SYNFORM** If you had not become a chemist, what other profession do you think you would have entered?

**Dr. C. Zhu** If I hadn't become a chemist, I might have gravitated toward being a doctor. The COVID-19 pandemic in recent years has made us deeply appreciate the importance of medical science. At this time, people often think about what they can contribute, and doctors are generally on the front line to save people's lives, which I find very admirable.

**SYNFORM** What is the most exciting aspect of your job, the one you like the most?

**Dr. C. Zhu** New discoveries in the lab are most exciting moments, although most of the time is spent with failure. Sometimes a new spot in TLC (thin-layer chromatography) or a new peak in the crude NMR spectrum is greatly attractive to me, because it indicates the formation of a new compound during the reaction.

*Matthew Fenske*



**Scheme 1** Dynamic kinetic resolution (DKR) and dynamic kinetic asymmetric transformations (DYKAT)

## Coming soon

— Literature Coverage

### Photochemical Diversification of Strong C(sp<sup>3</sup>)-H Bonds Enabled by Allyl Bromide and Sodium Fluoride

— Literature Coverage

### Synthesis of Calix[4]arene Appended Lactosylated G1 and Galactosylated G2 Generation Glycodendrimers Using a 'CuAAC' Click Approach

— Literature Coverage

### Copper-Enabled Photo-Sulfonylation of Aryl Halides Using Alkylsulfonates

## Further highlights

### **Synthesis** Review: Silyl Esters as Reactive Intermediates in Organic Synthesis

(by M. J. Adler and co-workers)

### **Synlett** Account: From Sweet Molecular Giants to Square Sugars and Vice Versa

(by P. Compain)

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