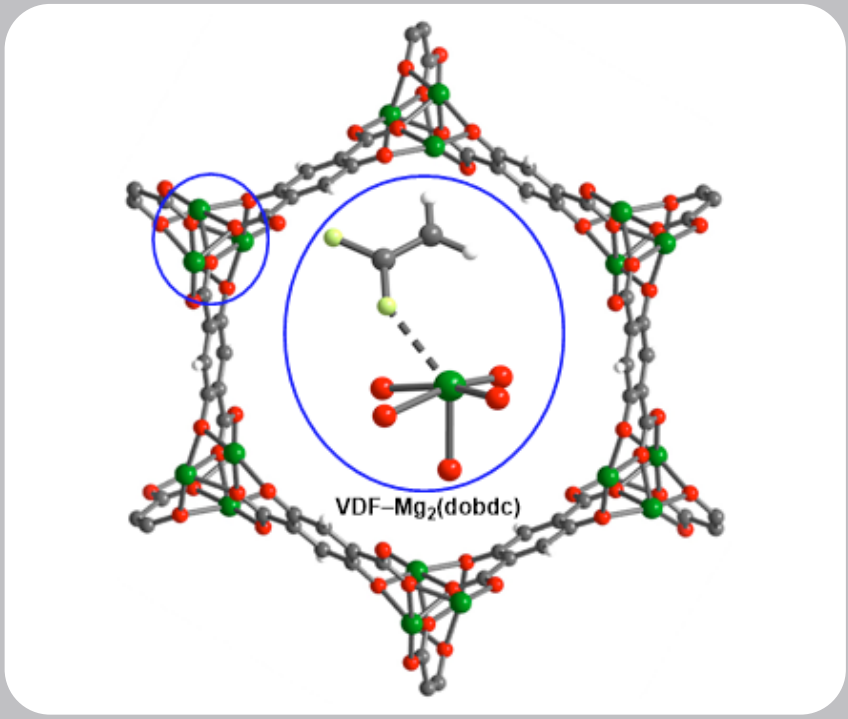
Synform

People, Trends and Views in Chemical Synthesis

2024/02

Handling Fluorinated Gases as Solid Reagents Using Metal–Organic Frameworks

Highlighted article by K. T. Keasler, M. E. Zick, E. E. Stacy, J. Kim, J.-H. Lee, L. Aeindartehran, T. Runčevski, P. J. Milner



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Dear Readers,

One of the aspects I am enjoying the most of my current period of secondment at an EU Agency is that holidays are real holidays, weekends are just for myself, and out-of-office time is truly hassle-free, whereas in academia most of the times holidays are just extra working days – free from heavy teaching loads, administrative responsibilities, and the mentorship of students – that we can dedicate to grants & article writing or catching up with the literature. It is well known that the pressure to publish, secure research grants, and excel in teaching often result in an overwhelming workload for academics. All those endless working hours are generally seen as necessary evil in a profession that remains highly fascinating and attractive to many. The problem is that juggling the diverse roles academics are tasked to take on can leave little room for personal and professional development, not to mention the lack of holidays and quality time to spend with family and friends, eventually fostering a sense of burnout and exhaustion which is all but uncommon among academics. Even though academics are well aware of the issues above, I am not sure we really appreciate the seriousness of the situation until we get a proper break, and I can now confirm from personal experience that the difference between an academic and a non-academic job is massive, especially in terms of enjoying a real break or actually being able to stop thinking about work outside working hours. Re-evaluating institutional expectations, fostering a culture of work-life balance, and providing adequate support for faculty members are among the urgent necessary measures that need to be put in place to safeguard the academic profession. Acknowledging the challenges posed by an excessive workload is crucially important for addressing a more sustainable and fulfilling academic environment, lowering the risk of losing talent in favour of alternative, and often better remunerated, non-academic jobs.

This February issue of SYNFORM stands out for featuring two Young Career Focus interviews – both involving recent Thieme Chemistry Journals Awardees – the first with Eduardo Anaya Plaza (Finland) and the second with Sukalyan Bhadra (India), who tell us about their professional and personal interests, elaborating on their research activities. The issue is opened by a Literature Coverage article on the ground-breaking work recently published in Science by the group of P. J. Milner (USA) for introducing fluorinated groups into organic molecules by harnessing a novel way of handling fluorinated gases as solid reagents using metal-organic frameworks. The second Literature Coverage article of the issue covers a novel strategy, developed by the group of C. Uyeda (USA), for generating and using nucleophilic dichloromethane-derived carbenes in organic synthesis.

Enjoy your reading! And please find a way to have proper breaks!!!

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Handling Fluorinated Gases as Solid Reagents Using Metal–Organic Frameworks

Science **2023**, *381*, 1455–1461

Fluorine is an essential element in medicine, agriculture, biomedical imaging, polymer chemistry, and beyond. However, organofluorine compounds are essentially xenobiotic – i.e. not available naturally – therefore their availability nearly exclusively relies on the capacity of organic chemists to develop suitable synthetic routes to these molecules. Substituting fluorine for ubiquitous hydrogen atoms can yield drug candidates with improved metabolic stability, bioavailability, and/or protein binding affinity. However, the extreme reactivity of fluorinating reagents complicates the installation of fluorinated functional groups. Novel methods for the mild and selective fluorination and fluoroalkylation of bioactive molecules are sorely needed, despite significant recent progress in the field.

Reagents amenable to the introduction of specialized fluorinated functional groups, such as fluorinated alkenes, remain few and far between. Additionally, fluorination depresses the boiling point of organic molecules, leading many fluorinated building blocks to be gases at room temperature. Compared to solids and liquids, gases are much more difficult to use in the laboratory, making high-throughput reaction discovery with gaseous reagents laborious and hazardous. Nonetheless, strategies for the safe handling of fluorinated gaseous commodity chemicals such as vinylidene fluoride (VDF) would facilitate the synthesis of fluorinated molecules with therapeutic potential.

"When working with gaseous reagents, most synthetic chemists rely on either complicated reaction setups or generation of the gas indirectly," said Professor Phillip J. Milner, from Cornell University (Ithaca, USA). "As a promising alternative, Ritter and co-workers demonstrated that halogen bonding interactions enable storage of the gas trifluoromethyl iodide (TFMI) as an easily handled liquid reagent. As a second source of insight, gas storage within porous solids – such as hydrogen storage relevant to hydrogen and fuel cell technologies – has been widely studied. In particular, metal–organic frameworks (MOFs) are next-generation materials that are used for a plethora of gas storage applications owing to their high internal surface areas and modular structures." Combining these two findings, Milner and co-workers hypothesized that fluorinated gases could be reversibly bound within MOFs via selective non-covalent interactions, allowing for their handling as stable solid reagents in the laboratory.

"To identify a material exhibiting both a high uptake capacity and a strong affinity towards VDF, we measured VDF uptake in over a dozen porous solids, including MOFs and zeolites," said Professor Milner. He continued: "This was accomplished by measuring VDF adsorption/desorption isotherms at three temperatures (30, 40, and 50 °C). Among the tested materials, the MOF Mg_2(dobdc) (dobdc^{4-} = 2,5-dioxidobenzene-1,4-dicarboxylate) possesses a high VDF capacity (7.95 mmol/g, 34 wt%) coupled with strong yet reversible binding (~40 kJ/mol). This framework is known to strongly bind numerous gases, including H_2 and CO_2, and we previously showed that it could be used to separate fluorinated molecules based on differing interactions with the Mg^{2+} sites in the MOF." Professor Milner explained that when kept cold (–20 °C) in a laboratory freezer, VDF can be stored within Mg_2(dobdc) with a half-life of over two weeks. He added: "Powder X-ray diffraction and magic angle spinning solid-state NMR studies support that the high affinity of Mg_2(dobdc) towards VDF and other fluorinated gases is due to favorable non-covalent Mg···F interactions within the pores of the MOF. Notably, this MOF can be prepared on a >100 gram scale at room temperature in water using inexpensive reagents, making it a scalable material for reaction discovery."

Professor Milner and co-workers demonstrated that VDF can be released from the MOF by simply submerging it in organic solvents such as *N,N*-dimethylformamide, diethyl ether, or toluene. "Interestingly, the rate of release was relatively independent of solvent polarity," explained Professor Milner. He added: "Furthermore, we demonstrated that gas-loaded MOFs can be encapsulated within wax to produce benchtop-stable reagents that only release gas when they are sonicated and broken up, but otherwise exhibit no gas loss even after 2 months. These wax capsules enable the safe handling and delivery of a wide range of gaseous reagents on demand, including VDF, TFMI, trifluoropropene (TFP), and hexafluoropropene (HFP)."

The reactivity of VDF under conditions relevant to organic synthesis is poorly understood. With a general strategy to handle fluorinated gases as solid reagents in hand, Professor Milner and co-workers employed these reagents in novel fluorovinylation and fluoroalkylation reactions (Scheme 1). "The use of gas–MOF reagents enabled us to develop the first defluorinative coupling of (hetero)aryl boronic acids and VDF

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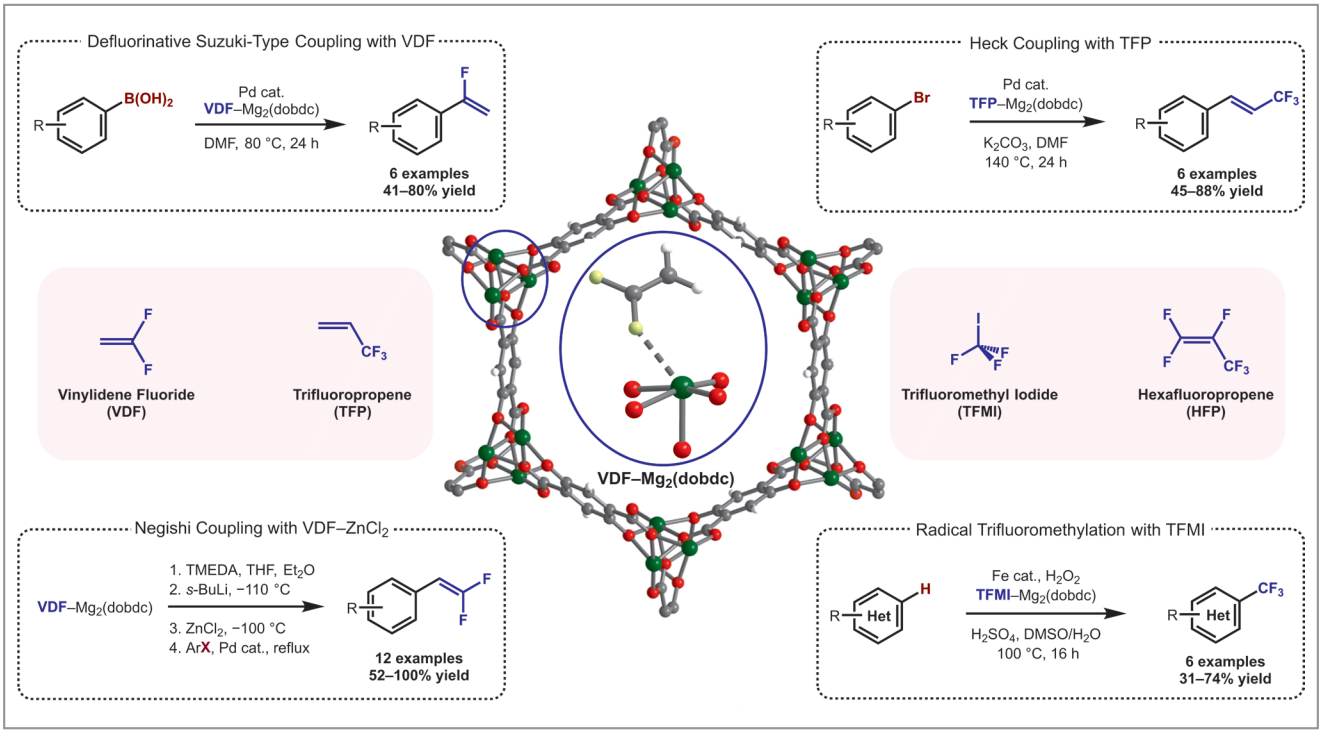
to produce valuable α-fluorostyrenes, which are considered amide bioisosteres in drug discovery," remarked Professor Milner. He continued: "In addition, we readily discovered that HFP also engages in this reaction without the need to design a new complicated reaction setup. Despite the recognized difficulty of defluorination reactions, most transition-metal catalysts studied to date follow this defluorinative pathway to produce partially fluorinated alkene products." To work around this selectivity challenge, Professor Milner and co-workers built upon previous reports and developed a protocol to deprotonate VDF with an organolithium base and transmetalate it onto Zn to produce reagents amenable to Pd-catalyzed Negishi couplings with (hetero)aryl halides. In this manner, a range of β,β-difluorostyrenes can be rapidly prepared.

Professor Milner said: "Given the success of VDF delivery, we next extended our exploration to the delivery of other fluorinated gases of synthetic interest. TFP could be released and engaged in Pd-catalyzed Heck couplings with (hetero) aryl halides to produce trifluoromethylated alkene-containing products. Likewise, TFMI can be released under Fenton-like conditions to produce trifluoromethyl radicals (CF_3·), which can be trapped via Minisci-like reactions with (hetero)arenes to yield trifluoromethylated products. Given the successful storage and release of a range of fluorinated gases using MOFs, this strategy represents a universal approach to simplifying reaction discovery using gaseous reagents."

"Moving forward, we will expand the scope of gases that can be stored within MOFs for reaction development, with an eye towards stabilizing more reactive halogenating gases," said Professor Milner, who concluded: "Likewise, we are studying the reactivity of underexplored fluorinated gases to enable a myriad of new synthetic transformations of interest to the pharmaceutical and agrochemical industries."



Scheme 1 Handling fluorinated gases as solid reagents using metal–organic frameworks to facilitate fluorovinylation and fluoroalkylation reactions

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About the authors

K. T. Keasler

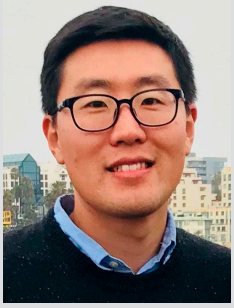
Kaitlyn T. Keasler received her A.B. in chemistry from Princeton University (USA) in 2020, where she conducted research in the laboratory of Prof. Paul Chirik. In the fall of 2020, she joined the laboratory of Prof. Phillip Milner at Cornell University (USA) as a Ph.D. student to explore the delivery of gaseous reagents for synthetic chemistry using porous materials. In 2022, she received the ACS Cornell Section Graduate Teaching Award and the Bristol Myers Squibb Graduate Fellowship.

Dr. M. E. Zick

Mary E. Zick graduated with a B.S. in chemistry from Siena College (USA) in 2018. She received her Ph.D. in 2023 from Cornell University (USA), where she worked in the laboratory of Prof. Phillip Milner. Her doctoral work focused on gas storage and liquid-phase and gas-phase separations in metal–organic frameworks and other materials. In 2023, she received the ACS Division of Inorganic Chemistry Young Investigator Award. She is currently a post-doctoral research associate in the laboratory of Prof. Bryan Boudouris at Purdue University (USA).

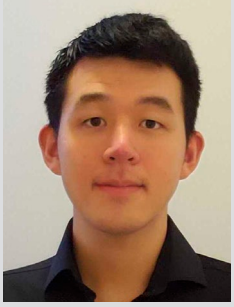
E. E. Stacy

Emily E. Stacy is from Pittstown, New Jersey (USA) and earned B.S. degrees in chemistry and biochemistry from Virginia Tech (USA). As an undergraduate, she worked in the laboratory of Prof. Paul Carlier on the synthesis of a new series of antimalarial treatments. She is currently a Ph.D. student in the laboratory of Prof. Phillip Milner at Cornell University (USA), where she studies catalysis enabled by metal–organic frameworks. She received the NSF Graduate Research Fellowship in 2023.



Dr. J-H. Lee

Jung-Hoon Lee received his B.Sc. degree from Pohang University of Science and Technology (POSTECH, Republic of Korea) before obtaining his Ph.D. at the same institution under the guidance of Professor Hyun M. Jang. His Ph.D. research mainly focused on understanding the origin of ferroelectricity in manganites and ferrites using density functional theory (DFT). He was a postdoctoral fellow at University of Cambridge (UK) with Prof. Antony K. Cheetham and Dr. Paul D. Bristowe and at UC Berkeley (USA) with Prof. Jeffrey B. Neaton, where he studied the electronic and structural properties of halide perovskites and MOFs. He joined the computational science research center at Korea Institute of Science and Technology (KIST, Republic of Korea) in 2019. His primary research to date has focused on the electronic structure of different materials, including both fundamental and applied aspects of DFT. Recently, he has conducted a research study to better understand the fundamental properties of nanoporous materials for gas capture and storage using high-performance computing techniques. More recently, he has focused on materials informatics and machine learning that accelerate materials discovery.



J. Kim

Jaehwan Kim graduated with and A.B. in chemistry from Princeton University (USA) in 2018, where he worked with Prof. Andrew Bocarsly and Prof. Buz Barstow (now at Cornell University, USA). He is currently a Ph.D. student in Prof. Phillip Milner's laboratory, where he is studying a range of heterogeneous redox-active organic materials as potential candidates for energy storage materials, and particularly their facile adaptability to alternative ion battery infrastructures such as sodium and potassium batteries. He has been selected as a 2024 PMSE Future Leader by the PMSE division of ACS.

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L. Aeindartehran

Lida Aeindartehran completed her bachelor's and master's degrees in chemical engineering at Babol Noshirvani University of Technology (NIT) in Iran. Lida joined Dr. Tomče Runčevski's group at Southern Methodist University (USA) as a graduate student in Fall 2020. Her research focuses on crystal engineering for new and improved formulations of pharmaceuticals. Her previous research focused on improving the solubility and taste of thiabendazole by making new crystal structures and applying acids as co-formers. At the moment, she is working on medicines for treating epilepsy.

Prof. T. Runčevski

Tomče Runčevski was born in Macedonia, where he finished his undergraduate studies in chemistry in 2011. He completed his Ph.D. at the Max Planck Institute (MPI) for Solid State Research in Stuttgart, Germany, working with Prof. Robert Dinnebier. He graduated in 2014 with honors, and he was awarded the Otto Hahn Medal of the Max Planck Society. After a one-year postdoctoral stay at the MPI, he joined the University of California, Berkeley (USA) and Lawrence Berkeley National Laboratory (USA) in 2015 as a postdoctoral researcher with Prof. Jeffrey Long. In 2018, he started his independent career at Southern Methodist University (USA) as an assistant professor of chemistry. He is currently a topic editor at the ACS journal Crystal Growth and Design. His research has been recognized with the NSF CAREER and ACS PRF awards.

Prof. P. J. Milner

Phillip J. Milner received his Ph.D. in organic chemistry from the Massachusetts Institute of Technology (MIT, USA) in 2015. At MIT, he worked under the supervision of Prof. Stephen Buchwald on Pd-catalyzed cross-coupling reactions as an NSF Graduate Research Fellow. From 2015–2018, he was an NIH Ruth L. Kirschstein Postdoctoral Fellow with Prof. Jeffrey Long at the University of California, Berkeley (USA), where his research focused on challenging separations using MOFs. In 2018, he joined the department of Chemistry and Chemical Biology at Cornell University (USA), where his research interests lie at the interface of organic, inorganic and materials chemistry. His research has been recognized with NSF CAREER, DOE Early Career, and Camille and Henry Dreyfus Teacher-Scholar awards.

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Young Career Focus: Dr. Eduardo Anaya Plaza (Aalto University, Finland)

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. Eduardo Anaya Plaza (Aalto University, Finland).

Biographical Sketch

Dr. E. A. Plaza

Eduardo Anaya Plaza obtained a PhD in organic chemistry in 2016 from Autonomous University of Madrid (Spain) and then moved as postdoctoral researcher to the University of Birmingham (UK). In 2018 he moved to Aalto University (Finland) with the help of the Marie Skłodowska-Curie-Actions (MSCA) grant. He established his research group, focused on photoactive organic materials, in late 2021 upon securing a total funding amount over 1.7 M€, which includes the prestigious Academy of Finland Research Fellowship. The group has published 19 articles in journals such as Nature Nanotechnology, Nature Communications, Angewandte Chemie International Edition or Advanced Materials. Additionally, the excellence of their research has been awarded with several recognitions including the Thieme Chemistry Journals Award in 2023.

INTERVIEW

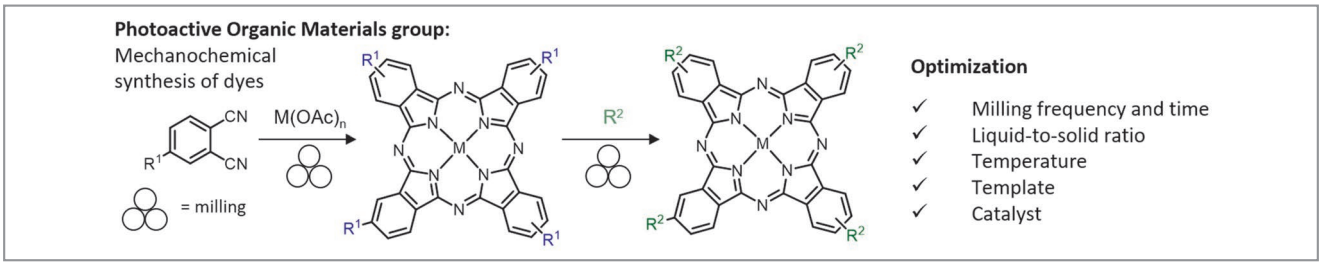
SYNFORM *What is the focus of your current research activity?*

Dr. E. A. Plaza I have always been dealing with the synthesis of dyes, as well as their properties in their aggregated/solid state, to then be exploited in a wide range of applications ranging from light-management technologies to phototherapies. This has brought me in recent years to the solid-state synthesis (e.g. mechanochemistry) of dyes (Scheme 1). Their large aromatic structures lead to poor solubilities, limiting the choice of solvents. That is easily overcome by this technique, opening the field to richer and more sustainable synthetic routes.

SYNFORM *When did you get interested in synthesis?*

Dr. E. A. Plaza During my undergrad at Autonomous University of Madrid, the research labs were on the way to class. From all of them, the one where I did my PhD had these big, colourful chromatography columns all over the place and I was immediately fascinated.

SYNFORM *What do you think about the modern role and prospects of organic synthesis?*



Scheme 1

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Dr. E. A. Plaza Organic synthesis has a capital role in our modern society providing from daily life items like cosmetic dyes for our clothes to life-saving antibiotics. While research in new synthetic methodologies is very much needed, pressing societal/environmental issues must be considered, especially when dealing with the scaling-up of processes. Therefore, new approaches like photochemistry, mechanochemistry or electrochemistry have a chance to make a bigger impact.

SYNFORM *Could you tell us more about your group's areas of research and your aims?*

Dr. E. A. Plaza The Photoactive Organic Materials group at Aalto University focuses on the synthesis and application of dyes for a vast array of technologies, ranging from light-emitting devices or solar cells, to phototherapeutic agents (Figure 1). We develop novel synthetic technologies based on mechanochemistry, as well as photoactive biomaterials and in the latest period small organic molecule-based solid-state emitters.

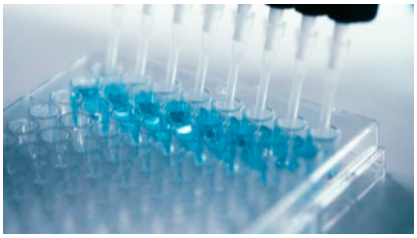

Figure 1 Application of phthalocyanines in biomedical applications, such as photodynamic therapy

SYNFORM *What is your most important scientific achievement to date and why?*

Dr. E. A. Plaza My biggest achievement up to date has been to create my research group in 2021. It has given me the independence to pursue my own research lines and interests, while educating the next generation of researchers.

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

Dr. E. A. Plaza I have been also very much attracted to cooking, which is basically the same with different starting materials.

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Nucleophilic Carbenes Derived from Dichloromethane

Angew. Chem. Int. Ed. **2023**, *62*, e202308913

The cyclopropyl ring is an important structural motif, featuring high ring strain and reactivity. Its unique properties make it a valuable building block in organic synthesis and drug design. Cyclopropyl rings are found in several pharmaceuticals, as they can introduce desirable properties into drug candidates and therapeutics. Cyclopropyl groups can also serve as bioisosteres for other functional groups, potentially improving drug potency or pharmacokinetics. Among cyclopropyl ring-forming reactions, catalytic alkene cyclopropanation reactions have a long history in organic synthesis, but most methods rely on diazoalkanes, which are energetic molecules that have significant safety concerns when used on commercial scales. For the past five years, the group of Professor Christopher Uyeda at Purdue University (West Lafayette, USA) has been interested in developing catalytic cyclopropanation reactions that can use readily available *gem*-dihaloalkanes as carbene precursors. "Our approach is inspired by a classic cyclopropanation method, the Simmons–Smith reaction," explained Professor Uyeda. He continued: "However, instead of stoichiometrically generating zinc carbenoids from CH_2I_2 and Zn, we are able to catalytically generate nickel carbene intermediates from a variety of *gem*-dihaloalkanes. One advantage of this approach is that the nickel catalyst is much more reactive than Zn metal, which allows us to use dichloromethane as the carbene precursor. Another advantage is that we are able to use chiral ligands to carry out highly enantioselective cyclopropanation reactions." Historically, developing catalytic enantioselective Simmons–Smith reactions has been challenging. Most examples use chiral Lewis acids and are restricted to allylic alcohol substrates. Professor Uyeda and his co-workers are hopeful that their approach using transition-metal catalysis will provide a more general solution to this synthetic problem (Figure 1).

"When we were first thinking about this reaction, we obtained some important clues from the literature," acknowledged Professor Uyeda. He explained further: "Decades ago, Hiroyoshi Kanai had shown that simple nickel salts enable cyclopropanation reactions of electron-deficient alkenes using typical Simmons–Smith reagents. This finding was intriguing because zinc carbenoids are known to be electrophilic and should be unreactive toward electron-deficient alkenes. Therefore, it was more likely that a nickel carbene of some kind was being generated in the reaction. Our contribution was to show that pyridine–bis(oxazoline) ligands could make the nickel-catalyzed cyclopropanation general across a broad range of substrate classes (Scheme 1). For example, we are able to access cyclopropanes bearing fluoroalkyl groups, sulfones, phosphonate esters, and nitriles, which are difficult

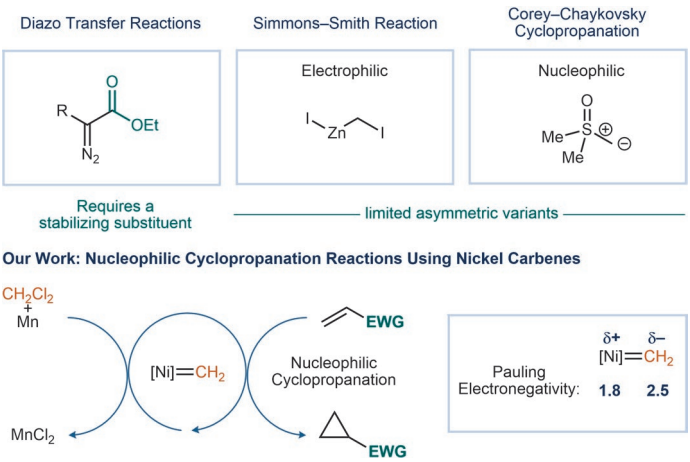

Figure 1 (Top) Established approaches to cyclopropanation based on diazoalkanes, zinc carbenoids, and sulfur ylides. (Bottom) Nickel-catalyzed cyclopropanation reactions of electron-deficient alkenes (EWG = electron-withdrawing group) using CH_2Cl_2 as a carbene precursor. The proposed nickel carbene intermediate has nucleophilic character due to polarization of the Ni–C bond.

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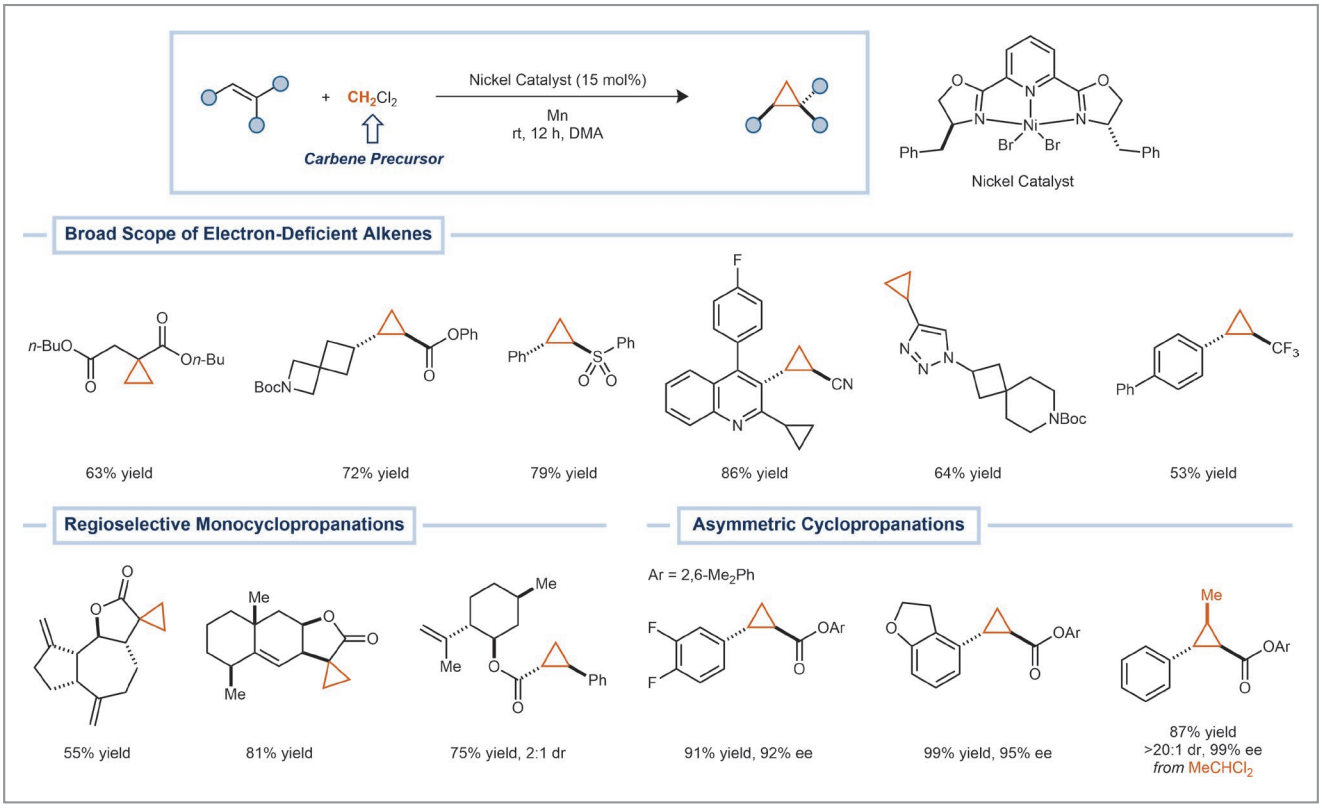
to prepare using other methods. For substrates that contain both electron-rich and electron-deficient alkenes, only the electron-deficient alkenes are cyclopropanated, demonstrating the nucleophilic character of the nickel carbene intermediate. Finally, we are able to take simple cinnamate esters and generate 2-aryl cyclopropanes that are found in pharmaceutical compounds."

Professor Uyeda concluded: "We hope that these studies will inspire a much broader investigation of transition-metal catalysts for reductive carbene transfer reactions using *gem*-dihaloalkanes. This is an underdeveloped approach to carbene generation, particularly when compared to the large body of literature on diazoalkane chemistry."



Scheme 1 A broad scope of electron-deficient alkenes undergo reductive cyclopropanation using a nickel catalyst. For complex polyalkenes, the most electron-deficient alkene is cyclopropanated with high regioselectivity. Chiral nickel catalysts enable highly enantioselective cyclopropanations of cinnamate derivatives.

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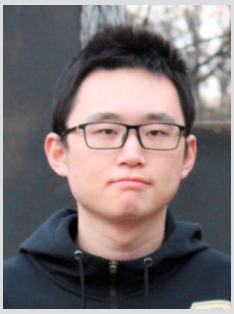
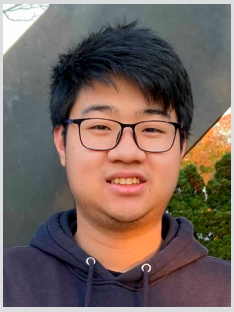
About the authors



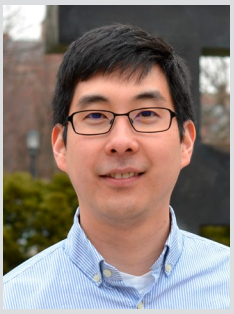
M. Liu

Mingxin Liu received his B.S. in chemistry at Jilin University (P. R. of China) in 2019. During his undergraduate studies, he spent a semester in Prof. Mingji Dai's group at Purdue University (USA) as a visiting student, where he worked on the total synthesis of natural products. Choosing to stay at Purdue University for graduate studies, he is currently a Ph.D. candidate under the guidance of Prof. Uyeda. His graduate research focuses on nickel-catalyzed carbene transfer reactions and reactivity studies of organonickel complexes.



N. Le

Nguyen Le received his B.S. in chemistry at Purdue University (USA) in 2023 where he carried out undergraduate research on nickel carbene chemistry in Prof. Christopher Uyeda's group. Currently, he is a Ph.D. student at Cornell University (USA) working under Prof. Song Lin's guidance on electrochemical oxidation catalysis.



Prof. C. Uyeda

Christopher Uyeda received his B.S. degree from Columbia University (USA), where he carried out undergraduate research on hydrophobically directed reactions with Prof. Ronald Breslow. He obtained his Ph.D. from Harvard University (USA) under the guidance of Prof. Eric Jacobsen. His thesis described the development of chiral hydrogen-bond donors for enantioselective Claisen rearrangements. He then carried out postdoctoral research on molecular electrocatalysts for solar fuel production with Prof. Jonas Peters. In 2013, he started his independent program at Purdue University (USA) and is currently the Richard B. Wetherill Professor of Chemistry. His research program focuses on developing catalytic carbene transfer reactions, studying catalytic processes at metal–metal bonds, and studying N=N coupling reactions for the synthesis of azo materials.

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Young Career Focus: Dr. Sukalyan Bhadra (CSIR – Central Salt & Marine Chemicals Research Institute, India)

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. Sukalyan Bhadra (CSIR – Central Salt & Marine Chemicals Research Institute, India).

Biographical Sketch

Dr. S. Bhadra

Sukalyan Bhadra received both B.Sc. and M.Sc. degrees in chemistry from the University of Calcutta, India and a Ph.D. degree from the Indian Association for the Cultivation of Science, India (Supervisor: Professor Brindaban C. Ranu). After two subsequent postdoctoral stints – at TU Kaiserslautern, Germany (Advisor: Professor Lukas J. Goossen) and Chubu University, Japan (Advisor: Professor Hisashi Yamamoto) – he began his independent research career in 2016 at CSIR-Central Salt and Marine Chemicals Research Institute Bhavnagar, India, where he currently works as a Senior Scientist. His research interest revolves around the development of novel methodologies towards metal-promoted organic transformations, cooperative catalysis, asymmetric catalysis and synthesis of fine chemicals and API molecules having industrial and/or marine relevance. He is the recipient of Green Talent Award (2010), JSPS Postdoctoral Fellowship (2013), DST-INSPIRE Faculty Award (2016) and Thieme Chemistry Journal Award (2023) among others.

INTERVIEW

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

Dr. S. Bhadra Our group works in the diverse field of organic synthesis and molecular catalysis including catalysis by transition metals and others, asymmetric catalysis, decarboxylative transformations and synthesis of drug molecules/intermediates having industrial and/or marine relevance. One of the major research areas of our group is catalytic α-functionalization of common organic compounds, e.g. acids, amides, esters, ketones, heterocycles etc. in a manner that is both step- and atom-economic, as well as sustainable. We also design ligands that work in a bio-inspired fashion towards metal-catalyzed α-functionalization reactions. In general, mild conditions, broad scope, excellent regio- and stereoselectivity, scalability, achieving bioactive compounds and synthetic intermediates constitute merits of our α-functionalization strategies. Further, we focus on the development of non-infringing and greener processes for perfumery chemicals and approved drugs including marine drugs.

SYNFORM *When did you get interested in synthesis?*

Dr. S. Bhadra I began to be fascinated by the art of organic synthesis in high school and undergraduate college, when organic chemistry was introduced in the curriculum. In particular, stereoselective synthesis of complex molecules having multiple stereogenic centres caught my attention, and I decided to study organic synthesis. Later, I pursued oganometallics in catalysis and their applications in organic synthesis, in which I continued my independent research career.

SYNFORM *What do you think about the modern role and prospects of organic synthesis?*

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Dr. S. Bhadra Invention of new classes of synthetic strategies is always important to upgrade traditional synthesis. In many cases, traditional synthesis yields unacceptable amounts of chemical wastes, thus increasing environmental threats. Furthermore, synthesis of complex molecules requires multistep processes. Modern science has nurtured traditional organic synthesis in many ways. For example, with the advent of catalytic C–H bond functionalization reactions, approaches involving organocatalysis, photo-redox catalysis, electro-catalysis, etc. have simplified the retrosynthesis of complex molecules. Likewise, automation, e.g. continuous-flow synthesis, has played a significant role in the synthesis of drug molecules. In addition, modern science has enabled the identification of numerous new molecules as drug candidates that have entered into clinical trials or have been approved. This has opened up new opportunities for the improvement of many lives.

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

Dr. S. Bhadra Outside the lab, I like to listen music and attend concerts. I love to listen to Indian classical music and instruments, in particular sitar. Sarod and violin also caught my interest.

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

Dr. S. Bhadra Inventing new reactions and designing new catalyst systems have always been a thrilling experience and an incredible venture. Establishing something that has never existed before is perhaps the toughest but most exciting job, particularly when it gives a concrete result. As synthetic chemists, we develop new chemical transformations and entities; however, the challenges remain to apply that chemistry in solving real life problems. To me, it is really exciting to develop some fundamental chemical strategy in the laboratory that can be taken forward to industry for scaling up towards the benefitting of mankind.

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Coming soon

Literature Coverage

Redox-Neutral Conversion of Ubiquitous P^V Sources to a Versatile PO_2^+ Phosphorylation Reagent

Literature Coverage

N-Heterocyclic Carbene- and Organic Photoredox-Catalysed *meta*-Selective Acylation of Electron-Rich Arenes

Literature Coverage

Chiral, Air-Stable, and Reliable Pd(0) Precatalysts Applicable to Asymmetric Allylic Alkylation Chemistry

Further highlights

Synthesis **Review: Recent Progress on the Zweifel Olefination: An Update**
(by X. Li, Q. Song)

Synlett **Account: Pt(II)-Bisacetylide 'Roller Wheels': Molecular Engineering towards Small Bandgap, High Crystallinity, and Controlled Triplet Exciton Processes**
(by Y. Qin)

Synfacts **Synfact of the Month in category "Polymer-Supported Synthesis": Cross-Coupling Reactions Catalyzed by Regularly Spaced Copper Atom Pairs on Polymeric Carbon Nitride**

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Editor
Matteo Zanda
C.N.R. – Istituto di Scienze e Tecnologie Chimiche (SCITEC)
Via Mancinelli, 7, 20131 Milano, Italy
Editorial Assistant: Alison M. Sage, synform@outlook.com

Editorial Office
Senior Director SYNTHESIS, SYNLETT, SYNFACTS:
Susanne Haak, susanne.haak@thieme.de
Scientific Editor:
Selena Boothroyd, selena.boothroyd@thieme.de
Development Editor:
Stefanie Baumann, stefanie.baumann@thieme.de
Editorial Assistant:
Sabine Heller, sabine.heller@thieme.de
Typesetting:
Ulrike Holzwarth, Büro für Gestaltung, Stuttgart
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