

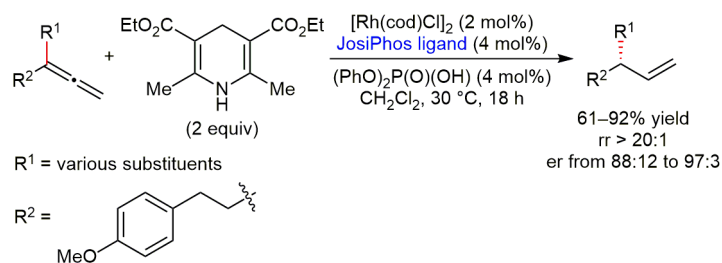
Synform

People, Trends and Views in Chemical Synthesis

2018/02

Enantioselective Semireduction of Allenes

Highlighted article by Z. Chen, V. M. Dong



Contact

Your opinion about Synform is welcome,
please correspond if you like:
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Thieme

Dear Readers,

Although this is the February issue's editorial, I am actually writing it soon after my return from the Festive season holidays. As usual, the reiterated Christmas and New Year's Eve celebrations have left a few extra kilograms distributed more or less equally on my body, with a clear predominance over the waist, which is currently requiring the use of a never-used-before hole on my belt. My first action for restoring the use of the original belt hole has been a draconian ban of anything even vaguely alcoholic, followed by a strict fruits and vegetable-based diet. But life is complicated, and to tell the truth last night I had some guests for dinner and – you know the situation – I actually had to cook ravioli followed by a roast, accompanied by a bottle of Italian red wine. Oh, and I forgot that Prosecco bottle we opened before dinner... And also those Italian chocolate and almond candies for dessert... and finally a dram of single malt to wash everything down... Sadly, the consequence is that this morning even the new belt hole seems to be inadequate to contain everything. But tomorrow is another day, my good intentions are still strong and this morning I feel incorruptible. Well, if it wasn't for those chocolate candies which are staring at me from the kitchen.... And those ravioli leftovers too.... OK, I may be weak when it comes to culinary matters, but I am strongly determined to continue with the traditional top-notch quality of our SYNFORM articles. And to demonstrate my incorruptibility on this subject I am now going to list the four outstanding stories of this new issue. The opener article is about a new method based on using borate esters for preparing complex amides, as recently devised by Tom Sheppard (UK). The runner up article covers the synthesis of diaryl and heterodiaryl sulfides via visible-light-promoted C–S cross-coupling developed by Garret Miyake (USA). The third contribution is a ground-breaking method

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for achieving the enantioselective partial reduction of allenes to terminal chiral olefins discovered by Vy Dong (USA). And to wrap up the issue, there is a Young Career Focus interview with Manuel van Gemmeren (Germany). Truly top-notch stuff, isn't it?

Oh what a nice surprise, there is also some Prosecco left from last night...

Enjoy your reading!



Contact

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

Borate Esters: Simple Catalysts for the Sustainable Synthesis of Complex Amides

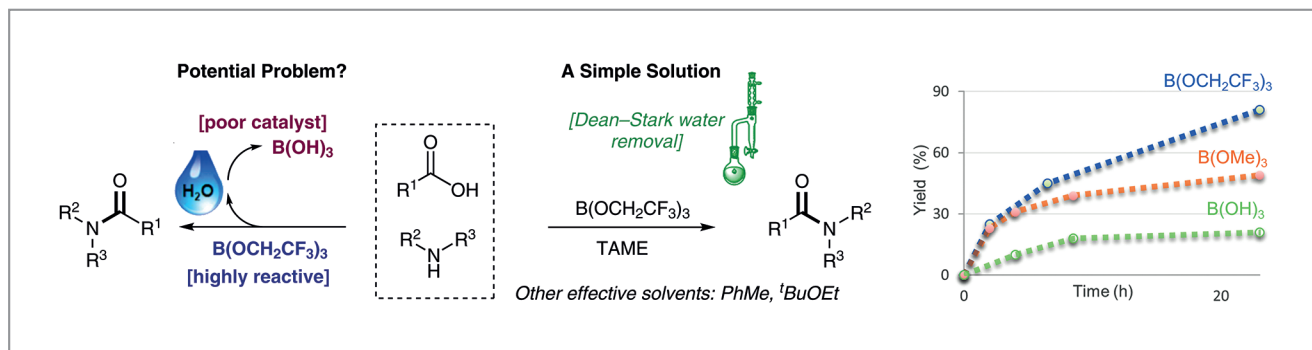
Sci. Adv. **2017**, *3*, e1701028

Direct amidation is an extremely important transformation in organic chemistry that is widely used by researchers throughout academia and industry, perhaps most significantly in the pharmaceutical industry. As a consequence of the inefficient stoichiometric methods that are used to achieve direct amidation reactions, there has been a renewed interest in the past 10–20 years in the development of catalysts for the reaction. In theory, an effective catalyst can enable the reaction to be achieved with only water being generated as a by-product. Catalytic approaches using boron-based systems or group IV metals have been particularly successful, but as yet these reactions suffer from significant drawbacks with high dilution conditions and large quantities of molecular sieves being required for efficient water removal. The substrate scope of these reactions is also limited with regard to the functionalised molecules required for pharmaceutical synthesis (such as functionalised polar molecules and heterocyclic compounds).

In previous work, the group of Professor Tom Sheppard at University College London (UK) developed the use of commercially available $\text{B}(\text{OCH}_2\text{CF}_3)_3$ as a stoichiometric reagent for direct amidation (*J. Org. Chem.* **2013**, *78*, 4512) and demonstrated that it is effective for amide formation with a wide range of highly functionalised amines and carboxylic acids (*Org. Biomol. Chem.* **2015**, *13*, 10888) including, remarkably, unprotected amino acids (*Chem. Commun.* **2016**, *52*, 8846). “We had hypothesised that borate esters would not be effective for use in catalytic quantities, as the water generated as the by-product of the amidation reaction should readily

hydrolyse the borate ester to boric acid, an amidation catalyst with low reactivity,” said Professor Sheppard. He continued: “By careful choice of reaction solvent, however, we found that efficient amidation catalysis could be achieved with a range of borate esters using a Dean–Stark water apparatus for continuous removal of water. The best solvent for the reaction was found to be tert-amyl methyl ether (TAME), which was recently identified as a greener ethereal solvent for use in process chemistry in the pharmaceutical industry (*Green Chem.* **2016**, *18*, 288). A plot of the reaction conversion against time with different catalysts clearly shows that borate esters are more effective than boric acid, and that *tris*-(2,2,2-trifluoroethyl) borate is more reactive than trimethyl borate.”

Remarkably, this catalytic amidation system proved to be more reactive than the group’s previous stoichiometric amidation method, with an unprecedented substrate scope. “Amides could be prepared from numerous primary/secondary amines, including poorly nucleophilic examples such as acyclic secondary amines, hindered anilines and a sulfonamide,” explained Marco Sabatini, the graduate student who developed the chemistry. He remarked: “In terms of the carboxylic acid component, amides derived from natural products and amino acids (both with/without protecting groups on the nitrogen!) were obtained in good to excellent yields.” The high reactivity of amino acid derivatives enabled a selection of dipeptides to be prepared and the development of a one-pot direct amidation/condensation of unprotected amino acids to give imidazolidinones. This latter method enabled the

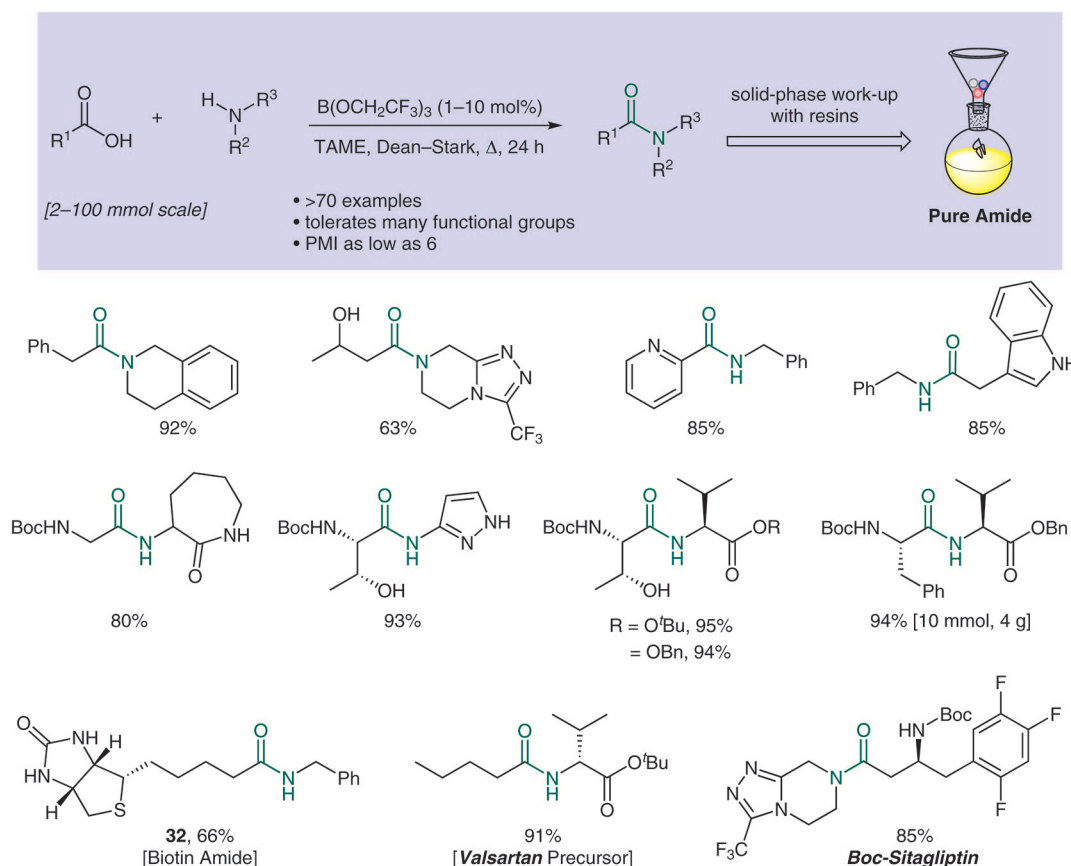


Scheme 1

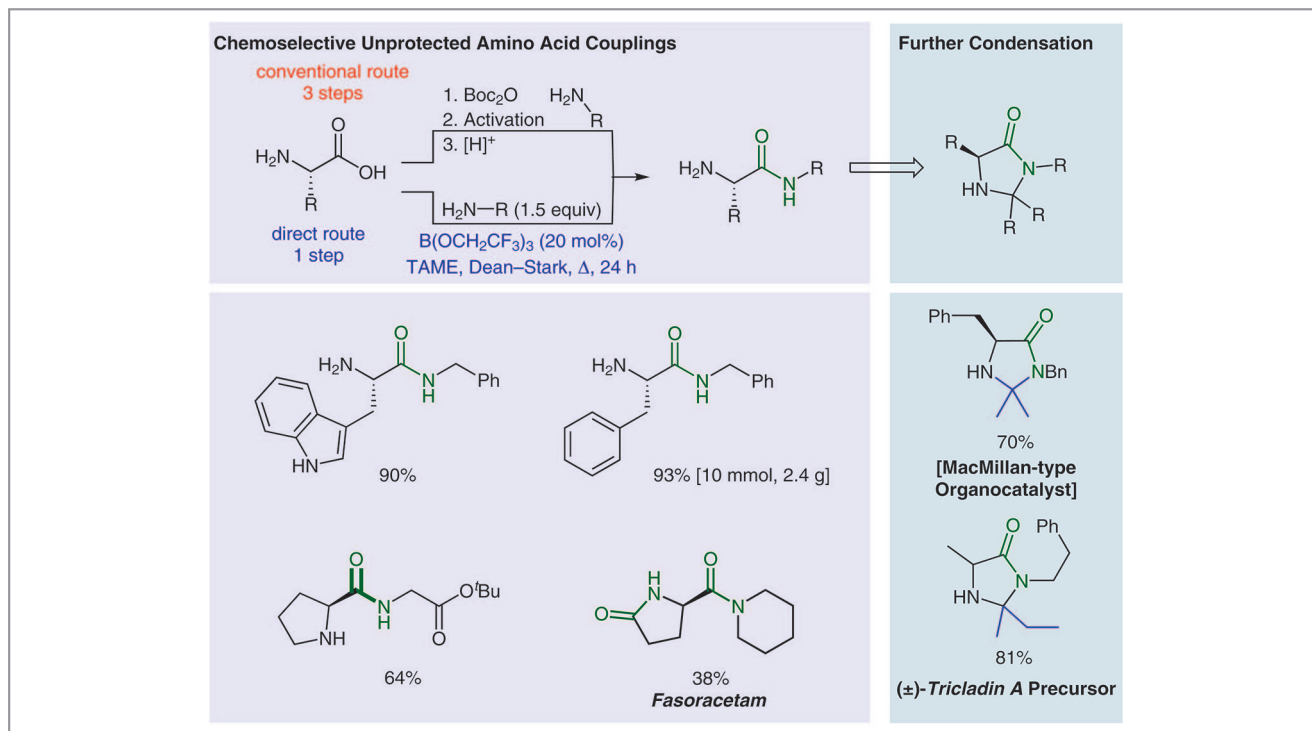
group to synthesise an organocatalyst, a chiral auxiliary and a natural product. Mr. Sabatini said: “Due to the importance of direct amidation in the pharmaceutical industry, we also demonstrated that the key amidation steps used in the synthesis of several APIs could be achieved efficiently using our catalytic method. Many of the amides were synthesised on multigram scale, and the majority of these amidation products could be purified using a simple solid-phase workup method which significantly reduces the solvent requirements of the process.”

Dr. Lee Boulton, an industrial collaborator on the project at GSK, explained that the concepts of green chemistry and sustainability have been the focus of the pharmaceutical industry for some time. “As a result, significant effort has been invested around improvements in efficiency and waste reduction in both research and development and full-scale manufacturing,” he added. “There are a number of measures to capture the overall sustainability of a process, but the challenge is

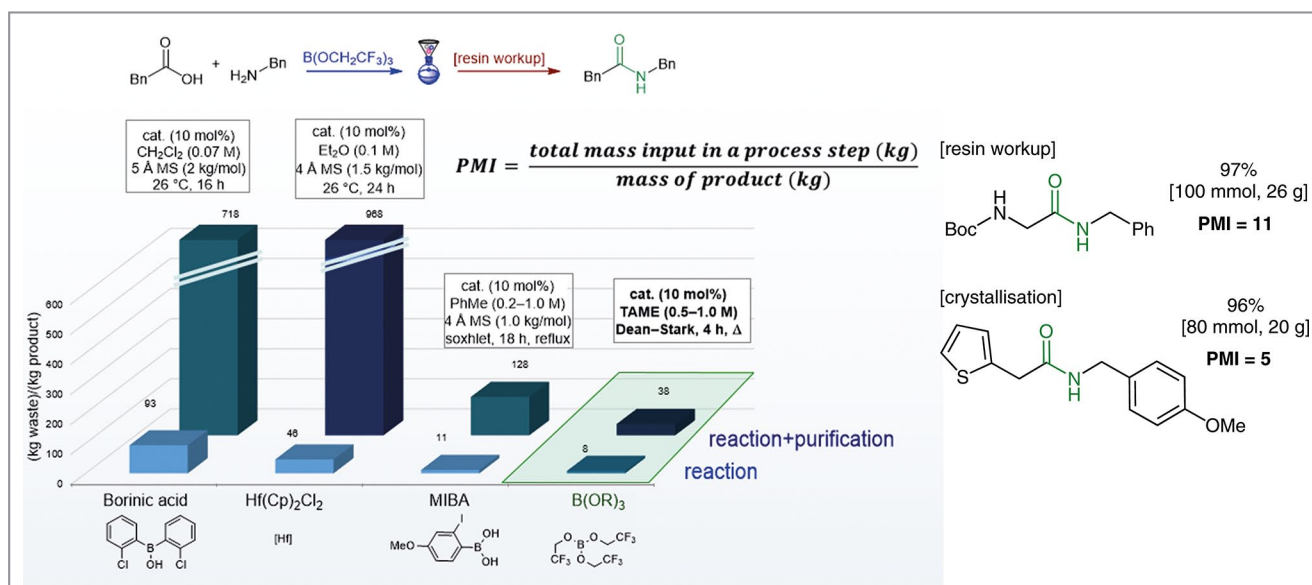
to identify key metrics that drive behaviours in greener, safer, innovative and more sustainable processes. The pharmaceutical industry, through the ACS Green Chemistry Round Table, has selected Process Mass Intensity (PMI) as a key benchmark when comparing such processes (*Org. Process Res. Dev.* **2011**, *15*, 912).” The PMI of a process is defined as the total mass of materials used to produce a specified mass of product. “In the ideal world this would approach unity. The use of PMI to compare our borate-catalysed system against current methods provides an excellent way to exemplify its green credentials,” remarked Professor Sheppard. He continued: “Our approach compares favourably to other recently reported catalytic amidation methods, as a consequence of both the reaction setup (higher concentration, no molecular sieves) and the efficient workup method (no aqueous workup needed).” He concluded: “Upon scaling the reaction up to 80–100 mmol (20–26 g of amide) further improvements to the efficiency could be



Scheme 2



Scheme 3



Scheme 4

made (PMI of 11 using solid-phase workup; PMI of 5 when the amide could be purified by direct crystallisation from the reaction mixture).” Dr. Boulton added: “This represents a highly efficient chemical process, especially for an amidation reac-

tion, and as a result GSK expect to add this method to their favoured reagent list for amide formation reactions.”

Matthew Farnish

About the authors



M. T. Sabatini

Marco Sabatini was born and raised in Garches (France). He received his MChem from the University of Bath (UK) in 2014, carrying out his research project under the supervision of Dr. Simon Lewis. He then joined Tom Sheppard's research group at University College London (UK) in 2014 as a graduate student, where he has been working on the development of novel catalytic methods for amide bond formation in collaboration with Lee Boulton at GlaxoSmithKline.



Dr. L. T. Boulton

Lee Boulton graduated from The University of Reading (UK) in 1992 and then went on to complete a PhD under the guidance of Dr. David Hodgson investigating the preparation of alkenylstannanes for use in cross-couplings. After postdoctoral studies at Scripps (USA) with Professor K. C. Nicolaou, looking at the preparation of the core structure of the Phomoidride series of compounds, he moved back to the UK and to Parke-Davis in Cambridge.

From Parke-Davis, Lee then moved to ChiroTech Technology and then onto GlaxoSmithKline in Stevenage (UK). Within the API Chemistry department at GSK, Lee has worked on a range of assets and is now focussing on embedding chemical technologies into development and manufacturing routes.



Prof. T. D. Sheppard

Tom Sheppard grew up in a small village in Lancashire (UK). He obtained his BA and MSci degrees from the University of Cambridge (UK) in 1999, carrying out a research project with Professor Ian Fleming. After working in the pharmaceutical industry at Glaxo-Wellcome for a year, he returned to the University of Cambridge for a PhD (2004) with Professor Steven Ley on the development of butane-2,3-diacetal desymmetrised glycolic acid.

He then moved to University College London (UK) to carry out postdoctoral research with Professor William Motherwell, working on novel zinc-mediated cyclopropanation reactions. In 2007, he was awarded an EPSRC Advanced Research Fellowship and appointed to a lectureship at University College London, and in 2013 he was promoted to Reader (Associate Professor) in Organic Chemistry. His research is focused on novel synthetic organic methodology, including organoboron chemistry, transition-metal catalysis and biocatalysis, with a growing emphasis on sustainable chemical processes.

Visible-Light-Promoted C–S Cross-Coupling via Intermolecular Charge Transfer

J. Am. Chem. Soc. **2017**, *139*, 13616–13619

The development of synthetic methods based on harnessing the power of visible light for promoting stereoselective reactions using photoredox catalysts is at the forefront of modern organic chemistry.

The group of Professor Garret Miyake at Colorado State University (Fort Collins, USA) and University of Colorado Boulder (USA) has been working toward developing strongly reducing organic photoredox catalysts that operate using visible light, in particular for organocatalyzed atom-transfer radical polymerization. “For example, we have shown that *N,N*-diaryl dihydrophenazines or *N*-arylphenoxazines are successful photoredox catalysts for the synthesis of polymers with controlled molecular weights and architectures,” explained Professor Miyake, continuing: “Additionally, these compounds have similar properties to precious metal ruthenium or iridium photoredox catalysts. We have also become interested in exploring if these organic molecules cannot only serve as sustainable alternatives to precious metal catalysts but potentially access even new reactivity, because these organic molecules can have even stronger reducing potentials, longer excited state lifetimes, while possessing high triplet quantum yields. In fact, these organic molecules can catalyze trifluoromethylation reactions or participate in dual photoredox coupling reactions that were previously only demonstrated with metal catalysts.”

Postdoctoral researcher Dr. Bin Liu started exploring the synthesis of aromatic thioethers because of their importance across a wide range of pharmaceuticals and natural products

(Figure 1). “In traditional approaches, aromatic thioethers are produced via the use of alkoxide bases, specific or air-sensitive ligands, high temperature, and transition-metal catalysts (Scheme 1),” confirmed Dr. Liu. “However, the high cost of typically employed precious transition metals (e.g. palladium) and limited functional group tolerance (e.g. due to the use of strong alkoxide bases) have imposed limitations on their use,” he said. Advances have been made in the production of aromatic thioethers via photoredox catalysis; however, these approaches either require UV irradiation or involve the use of nickel and iridium transition metals (Scheme 1).

Therefore, according to Professor Miyake, the continual development of environmentally friendly and atom-economical methods for constructing C–S bonds is of significant importance with broad impact across the areas of small-molecule synthesis and materials. “Liu’s investigation was performed using organic photoredox catalysts and he observed that C–S cross-coupled products could be obtained in high yields,” explained Professor Miyake. He continued: “However, his control experiments also revealed that the desired product was also isolated in high yield (97%) in the absence of the organic photoredox catalyst after one hour of white LED irradiation at room temperature. This result was clearly due to a novel reaction pathway leading to C–S bond formation.”

Another postdoctoral researcher, Dr. Chern-Hooi Lim, used density functional theory (DFT) calculations, in conjunction with UV–Vis spectroscopy, to support the formation of an EDA complex between the electron-rich thiolate anion and

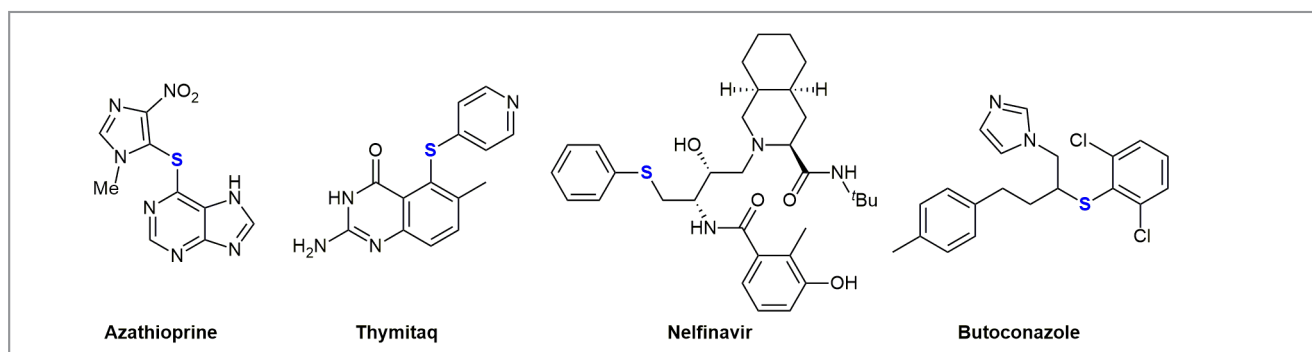
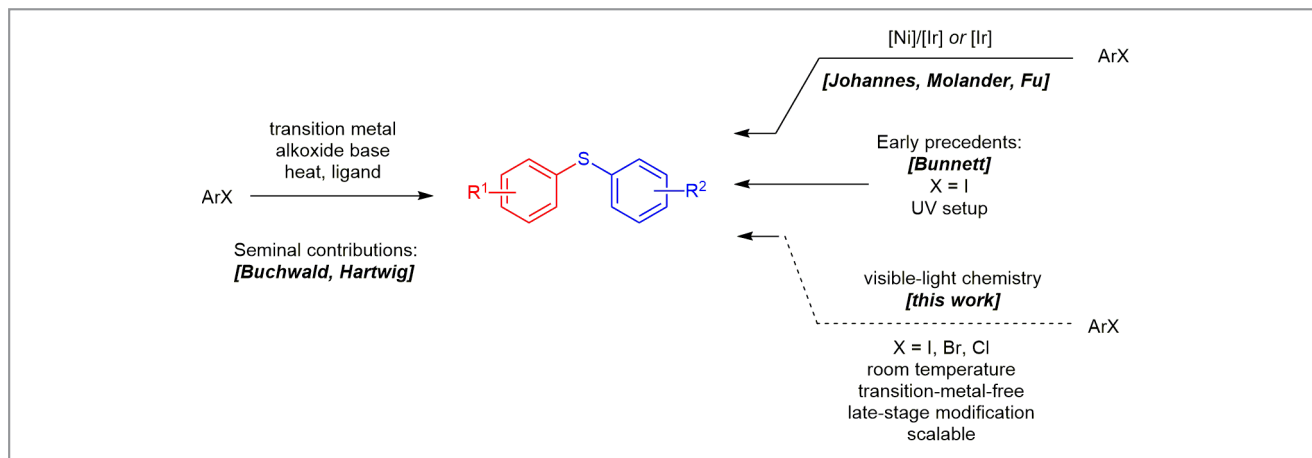


Figure 1 Thioether-containing medicinally relevant molecules



Scheme 1 Comparison of chemical methods to access aryl thioethers from aryl halides

the electron-poor aryl halide. “This EDA complex has UV-Vis absorption that extends into the visible region. Upon light absorption, an electron is transferred from the thiolate to the aryl halide species; this results in the formation of a thiyl radical and an aryl radical, which subsequently combine to form the C–S cross-coupled product,” explained Professor Miyake.

Expanding upon his original discovery, Dr. Liu developed this method consisting of a transition-metal-free cross-

coupling reaction between readily available aryl halides and aryl thiols to produce aromatic thioethers (>60 examples). Professor Miyake explained that the reaction is promoted by visible light via a proposed intermolecular charge-transfer mechanism. “This C–S cross-coupling methodology involves mild conditions: the reaction only requires the use of a mild base (e.g. Cs₂CO₃ and K₂CO₃) and the system is irradiated under visible light at room temperature,” remarked Professor

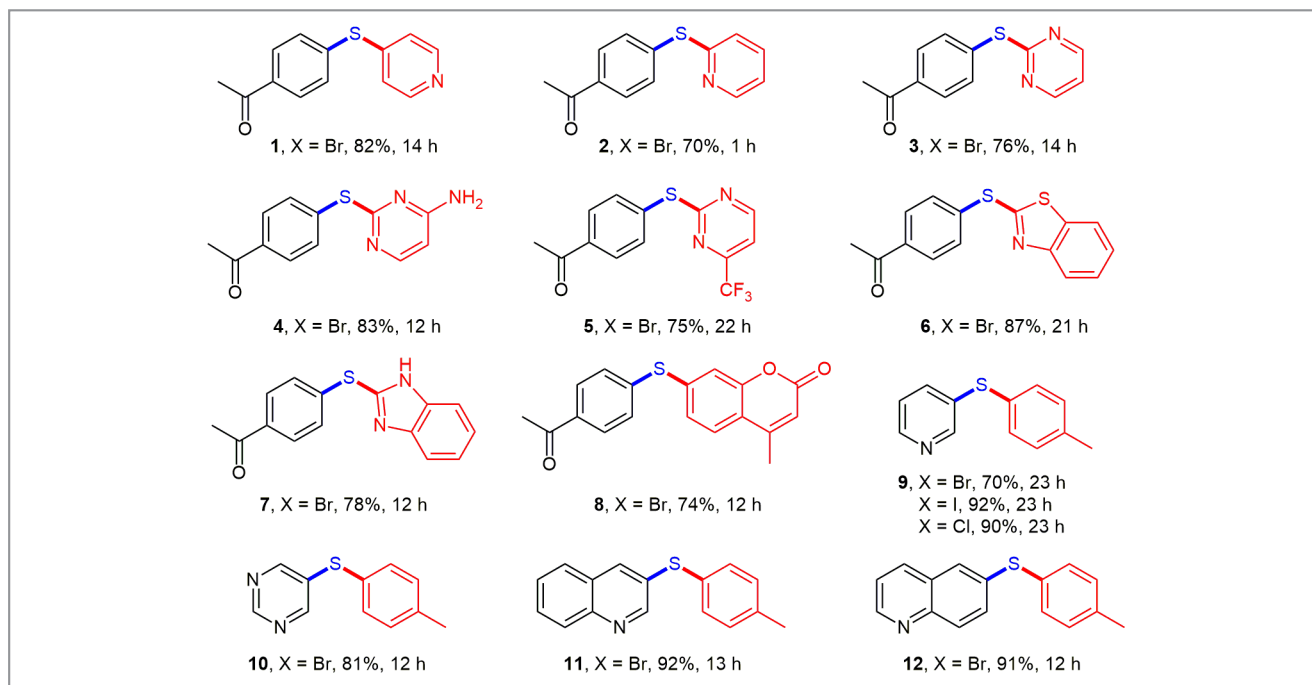


Figure 2 Scope of (hetero)arene coupling partners

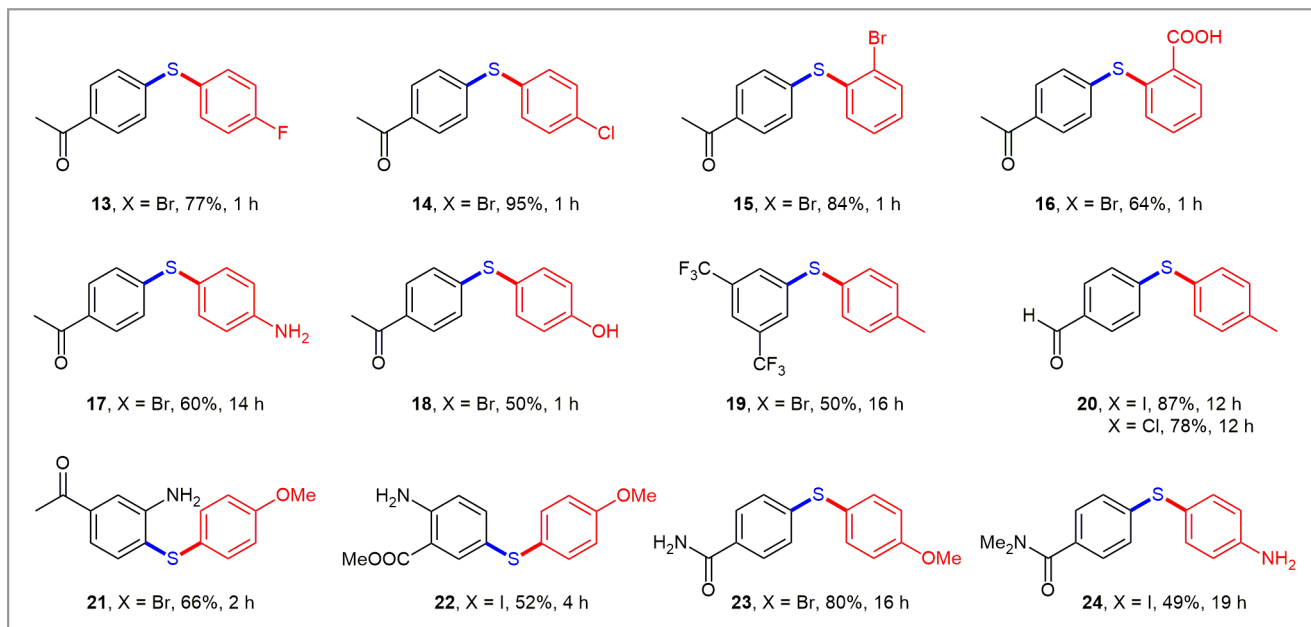


Figure 3 Selected examples of thiols and aryl halides

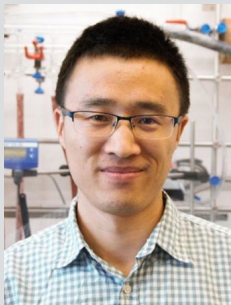
Miyake. "Furthermore, the use of mild and inorganic Cs_2CO_3 base has tolerated acidic functional groups such as amines, alcohols, and carboxylic acids."

With the optimized conditions in hand, the substrate scope and functional group tolerance of the reaction was investigated extensively. "Gratifyingly, the scope of the reaction is very broad (with over 60 examples) and is summarized here by a number of representative examples described in Figures 2 and 3," said Professor Miyake. He continued: "While this newly reported method represents a major advance in C–S cross-coupling methodology, limitations still exist in terms of alkyl thiols and electron-rich aryl halides that can be used."

Professor Miyake concluded: "We believe this synthetic procedure may find broad applications facilitating the access to new thioether-containing compounds in pharmaceutical, agrochemical, and materials sciences."

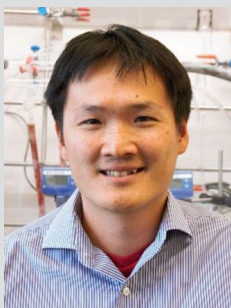
Matthew Farnish

About the authors



Dr. B. Liu

Bin Liu received his B.S. degree from Nanchang University (P. R. of China) in 2009. He then joined Professor Bing-Feng Shi's group in Zhejiang University (P. R. of China) and obtained his Ph.D. in organic chemistry in 2014. In the same year, he worked as a postdoctoral fellow with Professor Bing-Feng Shi at the same university. Since 2016, he has worked in Professor Miyake's group as a research fellow at the University of Colorado, Boulder (USA) and Colorado State University (USA).



Dr. C.-H. Lim

Chern-Hooi Lim is an NIH Ruth L. Kirschstein postdoctoral fellow working in the group of Professor Miyake at Colorado State University (USA). He earned his Ph.D. with Professor Charles Musgrave in the Chemical and Biological Engineering Department at the University of Colorado, Boulder (USA) in 2015. His current research interests include small-molecule and polymer synthesis via visible-light photoredox catalysis using organic photoredox catalysts. He applies combined quantum mechanical modeling and organic synthesis approaches to organic photoredox catalyst design and elucidates mechanisms in catalysis and photochemistry.



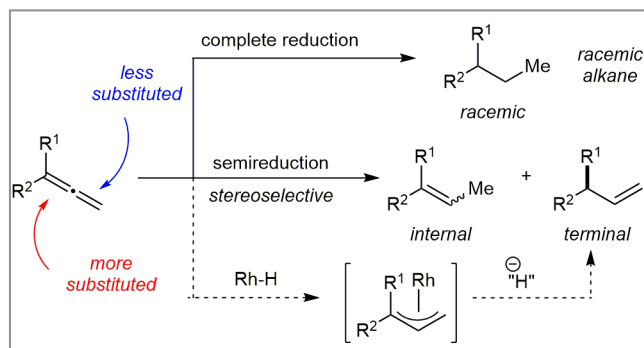
Prof. G. M. Miyake

Garret M. Miyake earned his B.S. in Chemistry from Pacific University (USA). He completed his Ph.D. studies with Eugene Chen at Colorado State University (USA) before conducting postdoctoral research with Robert Grubbs at the California Institute of Technology (USA). He began his independent career at the University of Colorado, Boulder (USA) in 2014 and returned to Colorado State University in 2017. The Miyake group currently has research interests focusing on catalysis, organocatalyzed atom-transfer radical polymerization, and the synthesis of block copolymers that self-assemble to photonic crystals. He has been awarded a Sloan Research Fellowship as well as the 2017 American Chemical Society's Division of Polymer Chemistry Mark Young Scholar Award.

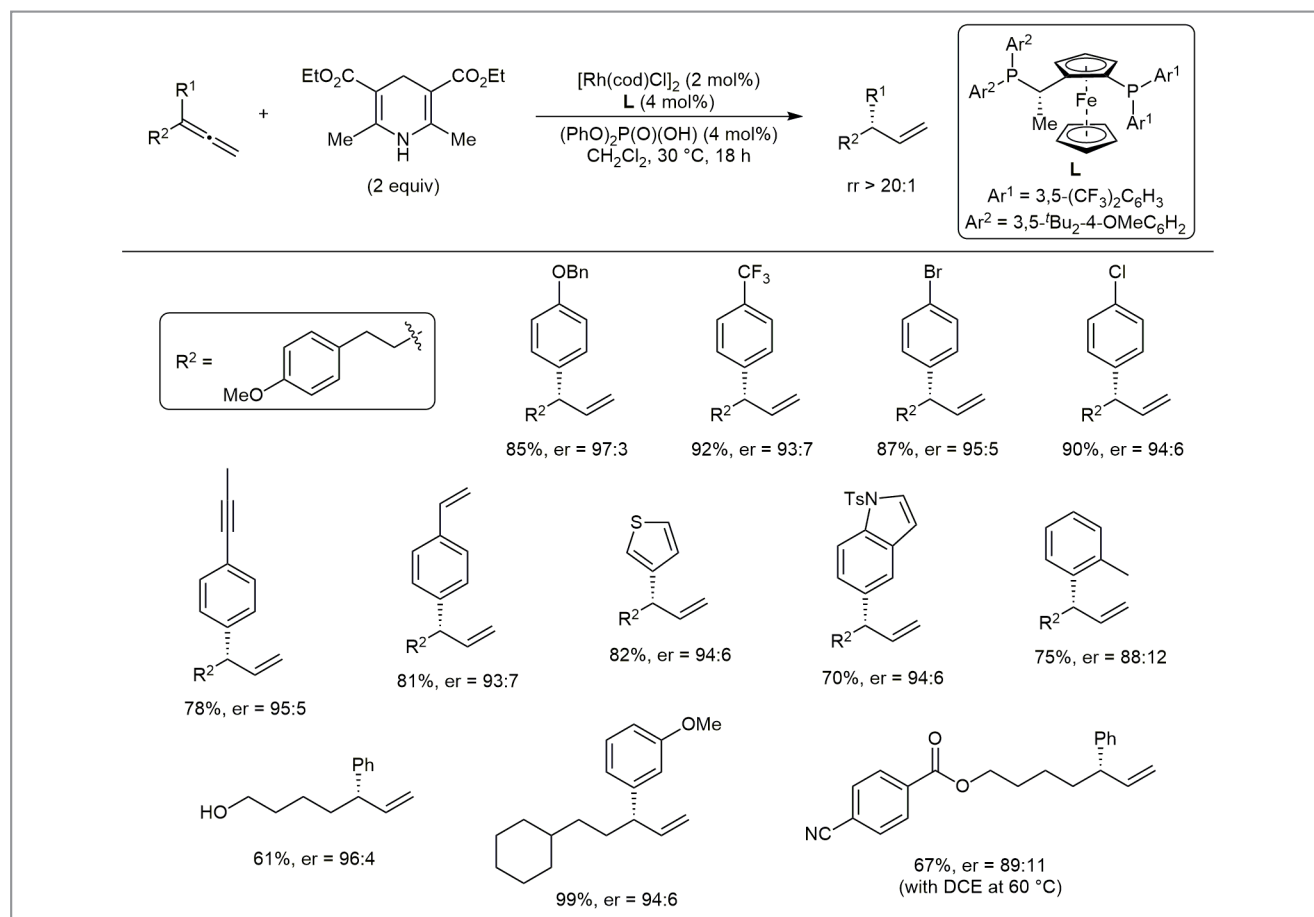
Enantioselective Semireduction of Allenes

Nat. Commun. 2017, 8, 784

Despite the numerous catalysts and reagents available for the reduction of a wide range of diverse functional groups, the selective reduction of allenes to terminal alkenes remains an unsolved challenge in organic synthesis. In fact, the few existing methods favor the formation of internal olefins. The group of Professor Vy M. Dong at the University of California, Irvine (USA) envisioned that a rhodium-hydride catalyst with a hydride nucleophile could give rise to an asymmetric allene semireduction, which could then lead to products bearing benzylic stereocenters that are common in medicinal chemistry. "It is known that Rh hydrides can insert into allenes to generate Rh-allyl intermediates," explained Professor Dong. She continued: "These species react with various nucleophiles



Scheme 1 Selectivity challenges in allene reduction and proposed method



Scheme 2 Selected substrate scope

to give branched products. In our semi-reduction, the nucleophile is a hydride. Nucleophilic hydride sources have been used in allylic substitutions with allylic electrophiles. Based on literature precedents demonstrating the feasibility of both steps, we were encouraged that our idea would also be feasible.”

The co-author of this *Nature Communications* paper, PhD student Zhiwei Chen, said: “We examined various hydride sources but found that a Hantzsch ester, synthetic analogue of NADH, afforded the highest regioselectivity. Other hydride sources, such as formic acid and silanes, are typically used in allylic substitutions.”

Professor Dong took up the story again: “Next, we found that a designer Josiphos ligand gave the products with excellent regioselectivities and high enantioselectivities without any isomerization of the allenes to the corresponding dienes. Lastly, our allene semi-reduction occurs chemoselectively in the presence of other functional groups, which could undergo reduction under typical hydrogenation conditions. Allenes bearing aryl halides, alkenes, alkynes, nitriles, and esters were selectively semi-reduced to the terminal alkenes.”

Professor Dong concluded: “Although this work represents a major advance in allene semi-reduction, the scope is currently limited to alkyl-aryl-disubstituted allenes. Future work will focus on expanding this method to include other allenes.”

Mattes Fank

About the authors



Z. Chen

Zhiwei Chen was born in Fujian province (P. R. of China) and grew up in Flushing, NY (USA). He obtained his bachelor's degree in chemistry from Queens College of CUNY (USA) in 2014 where he did undergraduate research with Yu Chen. He is currently a Ph.D. candidate in Vy Dong's group at the University of California, Irvine (USA). His research focuses on developing new Rh-catalyzed reactions.



V. M. Dong

Vy Dong was born in Big Spring, Texas (USA) and spent her early childhood in west Texas before moving with the family to Anaheim, California (USA). She graduated magna cum laude from UC Irvine (USA) where she majored in chemistry and completed an honor's project with Larry Overman. After graduation, she joined David MacMillan's group at UC Berkeley (USA), and then moved with his group to Caltech to complete her doctoral studies. Her Ph.D. thesis featured variants of the zwitterionic-Claisen rearrangement and a total synthesis of erythronolide B. As an NIH postdoctoral fellow, Vy pursued training in organometallic and supramolecular chemistry with Robert Bergman and Kenneth Raymond at Berkeley. She began her independent academic career at the University of Toronto (Canada), where she was promoted with tenure and named the Adrian Brook Professor. After six years in Canada, Vy returned to the USA to assume a professorship at her alma mater, UC Irvine. Professor Dong's research team is interested in new reaction methods, enantioselective catalysis, and natural product synthesis.

Young Career Focus: Dr. Manuel van Gemmeren (Westfälische Wilhelms-Universität Münster, Germany)

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. Manuel van Gemmeren (Westfälische Wilhelms-Universität Münster, Germany).

Biographical Sketch



Dr. M. van Gemmeren

Manuel van Gemmeren (né Mahlau) was born in Madrid (Spain) in 1985. He obtained his diploma in chemistry from the Albert-Ludwigs-Universität Freiburg (Germany) in 2010 and subsequently joined the group of Professor Benjamin List at the Max-Planck-Institut für Kohlenforschung (Mülheim an der Ruhr, Germany) for his doctoral studies, which he completed in 2014 (*summa cum laude*). In 2015, he joined the group of Professor Rubén Martín at the Institute of Chemical Research of Catalonia (ICIQ) in Tarragona (Spain). Since 2016 he has led an independent junior research group at the Westfälische Wilhelms-Universität (WWU) Münster (Germany). In 2017, he assumed a position as Otto-Hahn junior research group leader associated to the Max Planck Institute for Chemical Energy Conversion (CEC, Mülheim an der Ruhr, Germany). A collaboration between these institutions has enabled his group to remain based at the WWU Münster. His research has been supported by a number of awards and fellowships, such as the Kekulé Fellowship by the Fonds der Chemischen Industrie (2011–2014), the Feodor Lynen Research Fellowship of the Alexander von Humboldt Foundation (2015–2016), the Otto Hahn Medal and Award by the Max Planck Society (2015), the Liebig Fellowship by the Fonds der Chemischen Industrie (2016), and the Thieme Chemistry Journals Award (2017).

INTERVIEW

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

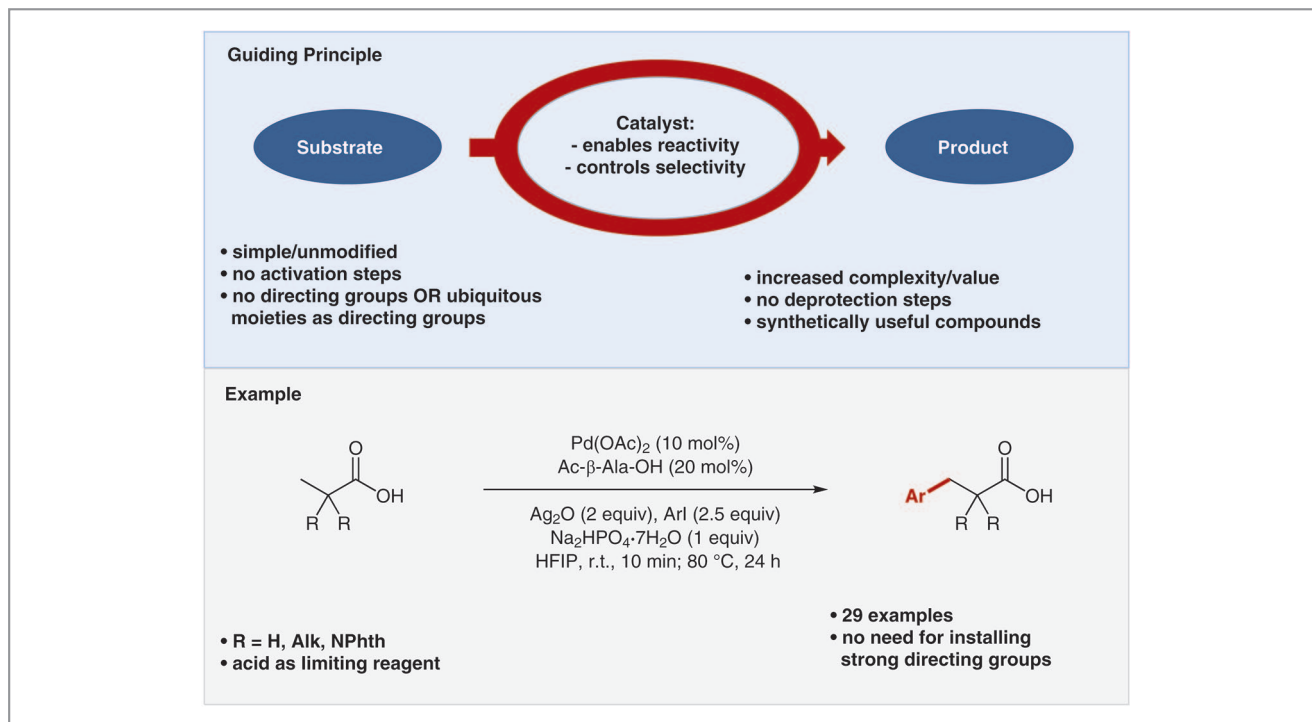
Dr. M. van Gemmeren During my doctoral and postdoctoral research I have repeatedly encountered situations where challenging reactions could only be enabled by novel catalysts. The research in my group is motivated by the observation that many synthetic methods are limited by the inherent reactivity of the respective substrates. This applies for example to C–H functionalization protocols, but also to cross-coupling methodologies and other well-established processes. We focus on the goal to, through the design of new catalysts and reagents, enable novel reactivities and/or selectivities in such cases.

SYNFORM *When did you get interested in synthesis?*

Dr. M. van Gemmeren I have been fascinated by organic synthesis ever since my first organic chemistry lecture. Synthesizing molecules from simpler starting materials and planning the necessary steps towards a complex target structure parallels playing with Lego, which I loved as a child. At the same time I quickly realized that synthesis is not only a fascinating challenge worth pursuing as an academic challenge and a form of creative expression, but also the key to accessing the resulting molecules, which are required by scientists in other research fields, for example for medicinal studies.

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

Dr. M. van Gemmeren I view organic synthesis as both a tool and an exciting research field. As a tool, organic synthesis, based on the current state of the art, can be used to make a



Scheme 1 Guiding principle and example for method development in the van Gemmeren group

multitude of products that are essential for virtually all parts of our everyday life, such as alimentation, sanitary applications, and medicine. As a research field, I am convinced that organic synthesis will continue to be instrumental in addressing many of the current and future challenges our society faces. For example, new synthetic technologies will be required in order to achieve the goals defined in the Paris Agreement, in crop protection to feed the growing world population, and for the transition to renewable chemical feedstocks and fuels.

SYNFORM Your research group is active in the area of new synthetic methodology development. Could you tell us more about your research and its aims?

Dr. M. van Gemmeren Our research is based on the guiding principle that a truly general synthetic approach to enable challenging reactivities and/or selectivities must be based on catalyst or reagent control, since a reliance on substrate control would automatically result in structural requirements on the substrate and thus reduce the usefulness of the protocol (Scheme 1). This implies that we target synthetic methods, which either do not require the use of directing groups, or rely on ubiquitous functionalities as directing groups. For

example, we have developed a protocol for the Pd-catalyzed $\beta\text{-C(sp}^3\text{)-H}$ arylation of aliphatic carboxylic acids that obviates the need for introducing a strongly coordinating directing group and nevertheless allows for the use of the carboxylic acid as the limiting reagent for the first time (*Chem. Eur. J.* **2017**, *23*, 17697).

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

Dr. M. van Gemmeren During my doctoral studies with Professor Benjamin List, I was involved in the use of Brønsted and Lewis acid catalysts in asymmetric counteranion-directed catalysis. One of the biggest challenges in this field has been the development of ever more active acid catalysts. Towards this goal, I developed a novel class of acid catalysts based on acidic C–H bonds which, in their silylated form, were later used to enable highly enantioselective Diels–Alder reactions of non-activated cinnamate esters for the first time (*Science* **2016**, *351*, 949).

Matthias Farnik

Coming soon

Literature Coverage

Organocatalytic Enantio- and Diastereoselective Cycloetherification via Dynamic Kinetic Resolution of Chiral Cyanohydrins

Literature Coverage

Highly Selective *gem*-Difluoropropargylation of Unactivated Alkylzinc Reagents Catalyzed by Nickel

Literature Coverage

Palladium-Catalyzed Dearomative *syn*-1,4-Carboamination

Further highlights

Synthesis Review: Synthesis of Monofluoroalkenes: A Leap Forward

(by J.-F. Paquin and co-workers)

Synlett Account: Recent Progress in Catalytic Enantioselective Desymmetrization of Prochiral Organosilanes for the Synthesis of Silicon-Stereogenic Compounds

(by R. Shintani)

Synfacts Synfact of the Month in category "Synthesis of Natural Products and Potential Drugs": Synthesis of an Inhibitor of Histone Lysine Demethylases KDM2/7

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