

## Young Career Focus: Dr. Markus D. Kärkäs (KTH Royal Institute of Technology, Sweden)

**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. Markus D. Kärkäs (KTH Royal Institute of Technology, Sweden).

### Biographical Sketch



Dr. M. D. Kärkäs

**Markus D. Kärkäs** received his MSc degree from Stockholm University (Sweden) in 2008. In the same year he began his PhD studies under the direction of Professor Björn Åkermark at Stockholm University. His thesis concerned the development of artificial water oxidation catalysts. After receiving his PhD degree in 2013, he joined Professor Corey Stephenson's research group at the University of Michigan (USA) as a postdoctoral fellow. His postdoctoral work focused on the development of photochemical methods for valorization of lignin. In late 2016, he returned to the Department of Organic Chemistry at Stockholm University. In August 2018, he joined the Department of Chemistry at KTH Royal Institute of Technology (Sweden) as an Assistant Professor and was promoted to Associate Professor in March 2022. His research interests include photocatalysis, organic electrocatalysis, and transition-metal catalysis. He was awarded a Bùrgenstock fellowship in 2018 and is a recipient of the 2022 Thieme Chemistry Journals Award.

are particularly interested in exploring sustainable technologies for accessing new chemical space within fundamental and applied research, in a more sustainable, safer, and cost-effective manner. Currently, research in our group focuses on addressing these challenges by leveraging the power of photocatalysis,<sup>1</sup> electrocatalysis<sup>2,3</sup> and transition-metal catalysis.<sup>4-7</sup> Especially, the former redox-modulating techniques provide the ability to selectively target functional groups in a molecule based on their different redox potentials. The use of low-energy visible light or electricity to mediate redox catalysis provides a platform for exploiting non-traditional bond constructions. This allows new bonds to be forged in a controlled and facile manner within the realm of green chemistry, affording a strategic paradigm for diversifying intermediates and final products.

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

**Dr. M. D. Kärkäs** My interest in chemistry began in high school. During my undergraduate studies at Stockholm University, I was particularly lucky to have excellent lecturers who sparked my curiosity in the subject. Initially, I did not intend to pursue PhD studies (and particularly not in organic chemistry). However, like most practitioners of the art, during my master's studies, I was introduced to some of the most elegant and complex solutions in organic chemistry and was mesmerized. I became enthralled in the challenge of organic synthesis even though many (most?) of the experiments failed. Organic synthesis is an art where design and problem-solving are crucial components. Therefore, I decided to pursue PhD studies at Stockholm University (supervised by Prof. Björn Åkermark). Later, I expanded my chemistry horizons through postdoctoral research at the University of Michigan (supervised by Prof. Corey Stephenson). Collectively, all these experiences provided me with the skills for starting my independent career. Finally, I have been very fortunate throughout my graduate and postdoctoral studies to have had advisors

### INTERVIEW

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

**Dr. M. D. Kärkäs** Our research team focuses on developing novel and efficient synthetic methods for accessing valuable organic frameworks from relatively simple building blocks. The long-term goal is to contribute new advances to the strategies and tactics employed in organic synthesis. We

who allowed me to carry out curiosity-driven research while also being incredibly supportive.

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

**Dr. M. D. Kärkäs** The modern world relies on organic synthesis in order to assemble the pharmaceuticals, agrochemicals and materials that are so pervasive in our modern society. Synthetic organic chemistry is a fascinating discipline that has been, and will continue to be, impactful across a range of research fields. Nevertheless, it will continue to draw inspiration from research advances in other disciplines, such as chemical biology, engineering, and physics. Organic synthesis is boundless and limited only by one's creativity, imagination, and persistence. The art of assembling and/or cleaving chemical bonds in a more controllable, effective, and sustainable manner continues to be an overarching objective. As a result, practitioners of organic synthesis have brought forward two of the most benign and versatile chemical reagents — electrons and photons. Albeit being broadly introduced recently, photocatalytic and electrochemical reaction manifolds have transformed the frontiers of forging bonds and expanded the repertoire of available activation modes. The development of more sustainable and cost-effective technologies for chemical processes could facilitate the transition from a fossil-based society to one that relies on renewable sources. Furthermore, automation and machine learning constitute additional areas that have the potential to fundamentally alter how synthetic chemists approach chemical challenges in the future. Ultimately, research advances in synthetic organic chemistry require synergy with other research disciplines, illuminating the essential role of collaborative, cross-disciplinary research endeavors.

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

**Dr. M. D. Kärkäs** As briefly mentioned above, our research team is pursuing three main topics: photocatalysis, electro-synthesis, and transition-metal catalysis (Scheme 1). Our research topics are constantly adapting with regard to the interests of our team members. Currently, free radical chemistry is a central theme as these intermediates can be leveraged to drive reactions that would otherwise be difficult to achieve through classical ionic/polar reaction manifolds. Traditionally, organic compounds have been assembled by reacting a pair of oppositely charged species — that is reacting a nucleophile, such as organomagnesium, with an electrophile, such as alkyl

halide. However, the direct activation of native chemical bonds, such as carbon–hydrogen (C–H) and carbon–oxygen (C–O) bonds, represents a powerful strategy for improving the atom- and step-economy as well as streamlining chemical synthesis. The development of such controlled, modular functionalization platforms would significantly expedite non-traditional bond constructions and expand the synthetic repertoire.

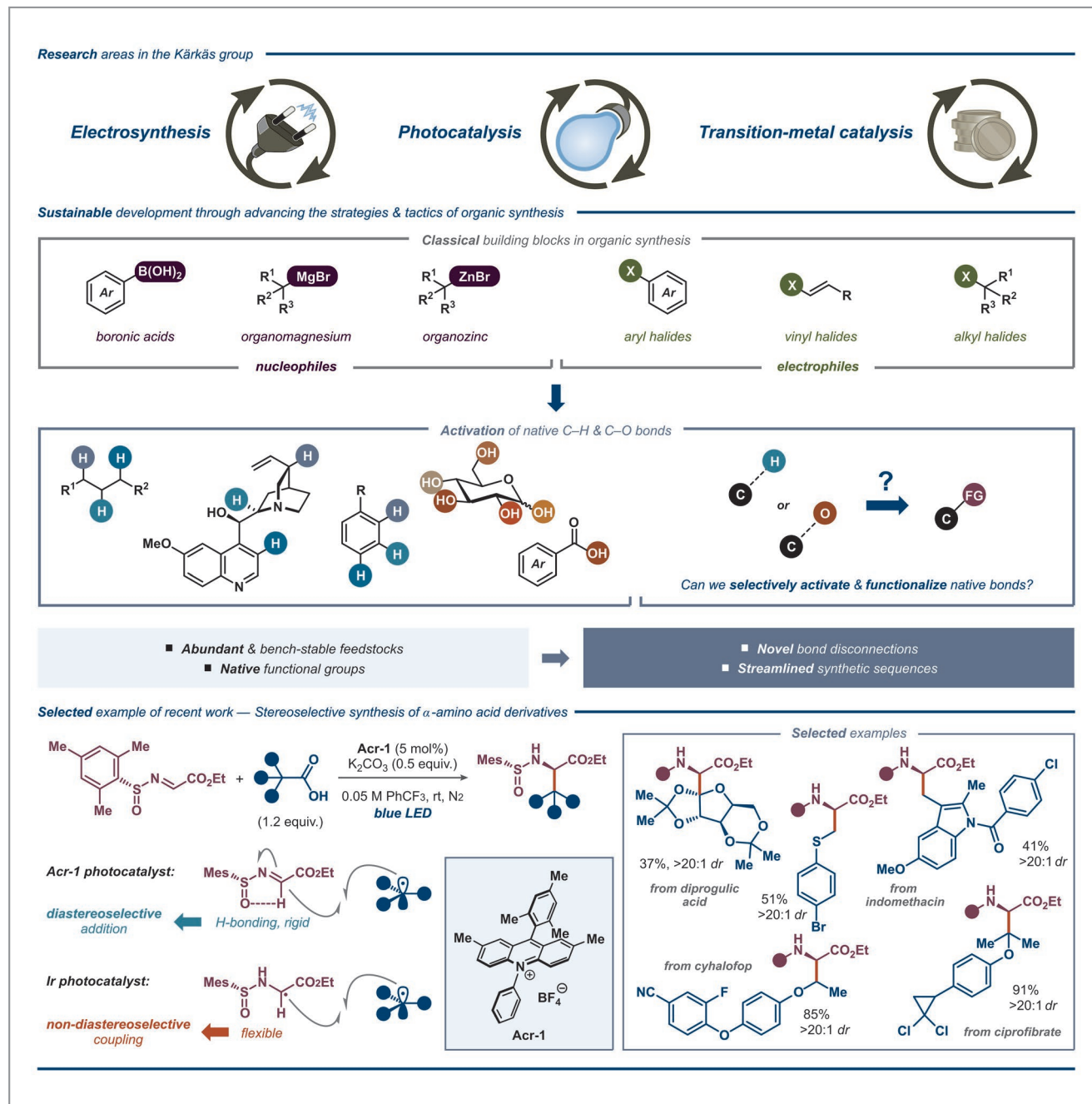
**SYNFORM** *What is your most important scientific achievement to date and why?*

**Dr. M. D. Kärkäs** Throughout the various stages of my research career, I am particularly pleased with some of the molecular single-site metal complexes, that were designed and developed during my PhD studies, which are capable of catalyzing water oxidation.<sup>8,9</sup> Furthermore, during my post-doctoral stay in the Stephenson group we were able to develop a redox-catalysis-based protocol for selective depolymerization of lignin, a recalcitrant and underexploited natural feedstock for aromatic commodity chemicals.<sup>10</sup> Recently, our research team initiated a project aiming at accessing unnatural  $\alpha$ -amino acids.<sup>11,12</sup> We designed a redox-neutral photoredox-enabled approach for the stereoselective synthesis of  $\alpha$ -amino acid derivatives (Scheme 1).<sup>13</sup> Here, unactivated carboxylic acids were employed as radical precursors and a metal-free acridinium catalyst was found to be the optimal photocatalyst. The developed protocol was applied to a variety of carboxylic acids and was shown to tolerate a diverse set of functionalities, including aliphatic and aromatic ethers and ketones; fluoro-, chloro-, and bromo-substituted aromatic substrates; aliphatic substrates containing  $\text{CF}_2$ ,  $\text{CF}_3$ , and  $\text{CCl}_2$  functionalities; and aryl cyanide- and alkyl aryl thioether-containing substrates. Gratifyingly, an array of pharmaceutically relevant compounds could also efficiently undergo decarboxylation, including cyhalofop, ciprofibrate, indomethacin, and diprogolic acid. Interestingly, intramolecular hydrogen bonding was not observed for the one-electron reduced species of the substrate ( $\alpha$ -amino radical), thereby providing a rationale for the observed poor stereoselectivity when the reaction was conducted with a more reducing iridium-based photocatalyst. In collaboration with the Dinér group, our team recently exploited photoredox catalysis for synthesis of spiro-compounds. Here, a dearomative annulation approach was harnessed, involving C–O bond activation of aromatic carboxylic acids. Delightfully, the protocol could be extended to intermolecular tandem sequences involving C–O bond cleavage, radical addition to an alkene and 5-*exo*-trig cyclization, yielding complex spirocyclic lactam scaffolds.<sup>14</sup>

Personally, I am extremely proud of the ambitious and skilled young scientists that I have had the pleasure of working with throughout the years. Attracting a group of enthusiastic and talented scientists to establish a completely new lab and monitoring their scientific endeavors is a privilege. Men-

toring is a privilege that one should take seriously. Thanks to the team members' curiosity and persistence, there are plenty of exciting projects in the pipeline.

*Mattias Forsell*



**Scheme 1** Research overview of the Kärkäs group

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