SYNLETT Best Paper Award 2015: Asymmetric Homogeneous Hydrogenation of 2-Pyridones

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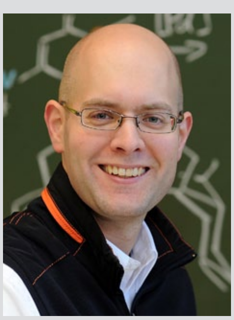
Background and Purpose. Thieme Chemistry and the Editors of SYNLETT and SYNTHESIS present the 'SYNTHESIS/SYNLETT Best Paper Awards'. These annual awards honor the authors of the best original research papers in each of the journals, considering their immediate impact on the field of chemical synthesis. Frank Glorius and his co-workers from the University of Münster (Germany) have won the inaugural SYNLETT Best Paper Award for the year 2015. The authors are honored for their work on the asymmetric homogeneous hydrogenation of 2-pyridones. Benjamin List, Editor-in-Chief of SYNLETT, praised the paper as a publication that "stands for what we expect from the best SYNLETT papers: To provide an original solution to a significant synthetic problem. The work of the Glorius team represents a new approach to the asymmetric hydrogenation of 2-pyridones and provides an elegant access to enantiopure 2-piperidones."
SYNFORM talked to Frank Glorius who was happy to share some background information regarding the prize-winning paper as well as his current research activities.

Biographical Sketch



Prof. F. Glorius

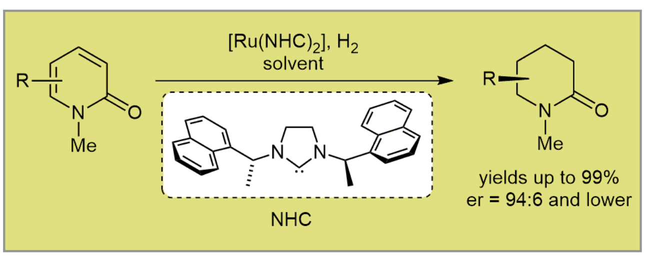
Frank Glorius was born in Germany in 1972 and educated in chemistry at the Universität Hannover (Germany), at Stanford University (USA) with Professor Paul A. Wender, at the Max-Planck-Institut für Kohlenforschung (Mülheim/Ruhr, Germany) and the Universität Basel (Switzerland) with Professor Andreas Pfaltz, and at Harvard University (USA) with Professor David A. Evans. In 2001, he began his independent research career at the Max-Planck-Institut für Kohlenforschung and in 2004 was promoted to Associate Professor for Organic Chemistry at the Philipps-Universität Marburg (Germany). Since 2007, he has been Full Professor at the Westfälische Wilhelms-Universität Münster. His research program focuses on the development of new concepts for catalysis and their implementation in organic synthesis. The group is especially interested in the chemistry of N-heterocyclic carbenes (NHCs), C–H activation, asymmetric arene hydrogenation, (asymmetric) NHC organocatalysis, photoredox catalysis, heterogeneous catalysis with common and with tailor-made, surface-modified nanoparticles, and the development of useful screening methodology. This work was acknowledged by a couple of distinguished awards, such as the OMCOS award, the Leibniz Award of the DFG (highest German research award), an ERC grant and the 2014 and 2015 Thomson Reuters Highly Cited Researcher acknowledgment.

INTERVIEW

SYNFORM *Could you highlight the value of your award-winning paper with respect to the state-of-the-art, potential or actual applications, and explain the origin, motivations and strategy used for conducting the research?*

Prof. F. Glorius Asymmetric transition-metal-catalyzed hydrogenation is a very attractive tool to produce enantiomerically pure organic molecules and, actually, in 2001 the Nobel Prize was given in part for this (to Ryoji Noyori and the late Robert Knowles). However, one great challenge remains: the efficient asymmetric hydrogenation of aromatic and heteroaromatic substrates. This kind of transformation would convert flat molecules into three-dimensional ones, a direction pharma industry would like to go with their drug candidates.

In recent years, several research groups around the world have contributed to this challenging transformation and great progress has been made. Still, the scope and efficiency of these transformations generally remain quite limited. In 2011, we were fortunate to develop a ruthenium–NHC based catalyst system that has proved to be a privileged system. Several different classes of heteroarenes could be successfully reduced, such as benzofurans, thiophenes, chromones and indolizines. In the SYNLETT paper highlighted here, we reported our results on the asymmetric hydrogenation of 2-pyridones, nice precursors towards piperidine product motifs (2-piperidones, specifically). But to be fair, many things still need to be improved and we feel that a deeper understanding of the catalyst system would be the ideal next step. We hope that this work will inspire other groups and especially the younger generation to address this long-standing synthetic challenge.

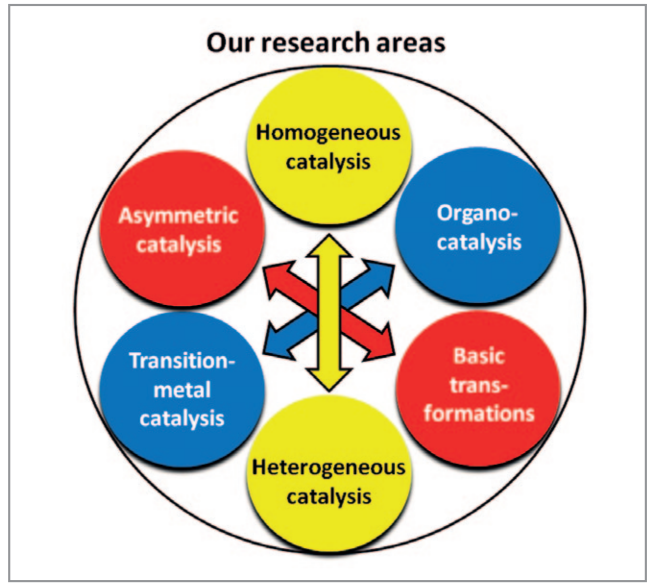


SYNFORM *What is the focus of your current research activity, both related to the award paper and in general?*

Prof. F. Glorius Characteristic for the Glorius group is the broad range of topics within the field of catalysis (see image below). In terms of this kind of hydrogenation technology, we try to elucidate the structure and mode of action of the active catalyst – a truly challenging endeavor. In addition, the group is also very active in other fields of NHC catalysis, including organocatalysis and the use of NHCs for the modification of catalytically active metal nanoparticle surfaces. Moreover, we also have very active research programs on C–H activation chemistry [utilizing Rh(III) and Co(III) catalysts] and photocatalysis, especially cooperative systems. Finally, we also try to develop smart screening technologies, beneficial for many different fields.

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

Prof. F. Glorius The field of organic chemistry is up and running. We can be proud of the many achievements of the past, but I also project a glorious future, since (organic) chemistry is the central science! But I am very critical of the increasing pressure from politicians and society (maybe also by fellow scientists?) to do 'something useful', pushing scientists more towards applied research. Don't get me wrong, applied research is extremely important and has its place, but we have to leave room for exploratory, basic research. Freedom of scientists is so important, because we are at our best when we can do what we want. Wherever I can, I try to advertise for freedom in science/chemistry, because I am convinced that this will lead to truly spectacular breakthroughs and game-changing developments.



The Glorius Group *Left:* official group photo. “Everyone is alert and looks strong: strong individual scientists enjoying freedom of research,” commented Professor Glorius.” *Right:* Photo taken during the preparation for the official photo. “It is spontaneous, a serendipitous photo. It represents the interaction between the group members,” said Professor Glorius, who concluded: “The two photos displayed sequentially give you the impression of a movie. I like this combination very much. The interplay between freedom and interaction is something I am advocating for and I try to bring it to life in my group.”