

## SYNTHESIS Best Paper Award 2016: Enantioselective Vicinal Diacetoxylation of Alkenes under Chiral Iodine(III) Catalysis

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**Background.** Thieme Chemistry and the Editors of SYNTHESIS and SYNLETT 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.

Kilian Muñoz and Thorsten H. Wöste from the Catalan Institution for Research and Advanced Studies and The Barcelona Institute of Science and Technology (Spain) are the recipients of the SYNTHESIS Best Paper Award 2016. The authors are recognized for their work on the enantioselective vicinal diacetoxylation of alkenes under chiral iodine(III) catalysis. Paul Knochel, Editor-in-Chief of SYNTHESIS, commented: “The development of new catalytic asymmetric synthesis of chiral molecules is especially important for pharmaceutical and fine chemistry in general. Kilian Muñoz and Thorsten Wöste have reported a very mild method for converting styrene and a range of related functionalized styrene derivatives into the corresponding vicinal diacetoxo derivatives with excellent enantioselectivities (up to 96% ee). The reactions proceed via a hypervalent iodine(III) catalytic species generated in situ. This enantioselective method is not only important by itself, but the results reported in this SYNTHESIS Best Paper 2016 will be very instructive for the future development of similar hypervalent iodine catalyzed difunctionalizations of alkenes. This work will be of interest both for synthetic applications as well as for the comprehension of iodine(I/III)-catalyzed enantioselective addition.”

SYNFORM talked to Kilian Muñoz who was happy to share some background information regarding the prize-winning paper as well as current research activities ongoing in his group.

### Biographical Sketch



Prof. Dr. K. Muñoz

**Kilian Muñoz** was born in 1970 in Hildesheim (Germany). He studied chemistry at the Universities of Hannover (Germany) and Oviedo (Spain) and at Imperial College, London (UK), and received a Doctorate in Chemistry from the RWTH Aachen (Germany) in 1998 working with Professor Carsten Bolm. He was a postdoctoral associate with Professor Ryoji Noyori at Nagoya University (Japan) in 1999/2000. He started his independent research in 2001 at Bonn University (Germany), before accepting a full professorship at Strasbourg University (France). He

was elected as a junior member to the Institut Universitaire de France in 2008. Kilian Muñoz moved to his present position at ICIQ in Tarragona (Spain) in 2009. Since 2010 he has also been an ICREA research professor. His research throughout the past decade has dealt with the development of new processes in the area of amination chemistry, in particular with the oxidative amination of alkenes.

Outside the laboratory, he spends time on modern (European) literature and arts, and enjoys good food and wine.

## 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. Dr. K. Muñiz** The 1,2-diol unit is a concurrent motif in numerous small molecules with biological, pharmaceutical and medicinal impact. One of the most appropriate approaches to their synthesis consists of a single-step oxidative transformation of alkenes as widely available starting materials. If conducted in an asymmetric fashion, such a reaction builds defined three-dimensional architectures from flat sources. The dominating process is the area that still belongs to osmium catalysis with chiral alkaloid ligands, which was pioneered by K. Barry Sharpless and recognized with a share in the 2001 Nobel Prize. The idea of exploring chiral non-racemic iodine(III) reagents to achieve vicinal dioxygenation of alkenes was initially conceived by Thomas Wirth in pioneering studies from the 1990s and extended by Morifumi Fujita. We initially became interested in these types of reagents within our work on the related 1,2-diamination of alkenes and suddenly found ourselves involved in the question of how to pursue asymmetric reactions catalytic in iodine(III). Together with Kazuaki Ishihara we have explored the working mode of related catalysts and identified supramolecular hydrogen bonding as a powerful tool for the design of aryl iodine(III) catalysts (Figure 1).

The results reported in the SYNTHESIS paper are based on a postdoctoral stay of Thorsten Wöste, who joined my laboratory after a Doctorate with Professor Martin Oestreich. He

was able to develop well-balanced conditions that use electrophilic fluorine reagents for the selective oxidation of the iodine center and to prevent any possible achiral background reaction. Our publication also devotes some effort to understanding the underlying mechanistic pathways that are involved in the diacetoxylation reaction. Knowledge of competing pathways is obviously very important, when one aims to develop new transformations or to improve existing ones. In the present case, we identified three different pathways that are involved in the formation of the final diacetoxylation product – luckily they all provide the same major enantiomer!

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

**Prof. Dr. K. Muñiz** My group focuses on oxidative amination reactions in general and vicinal diamination reactions in particular. If there is a challenge in amination, I am interested! I find C–N bond-forming events a stimulating field of research, since, unlike many other organic transformations, there is no real precedent in Nature. Traditionally, we have worked a lot on transition-metal catalysis, particularly high-oxidation-state palladium catalysts. Recently, we have explored the redox properties of iodine compounds which provide catalysts of unique economic and ecological appeal. In combination with other concepts such as photochemistry, this field currently widens into an exciting playground. Among my favorites of our recent accomplishments is an iodine-catalyzed intramolecular C–H amination initiated by light that forms pyrrolidines (Figure 2). This is the first realization of a catalytic version of the famous Hofmann–Löffler reaction, more than a century after its general development.

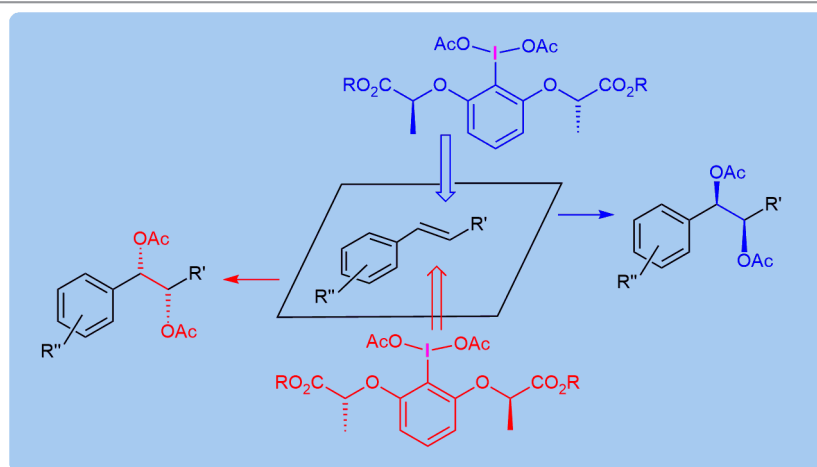


Figure 1

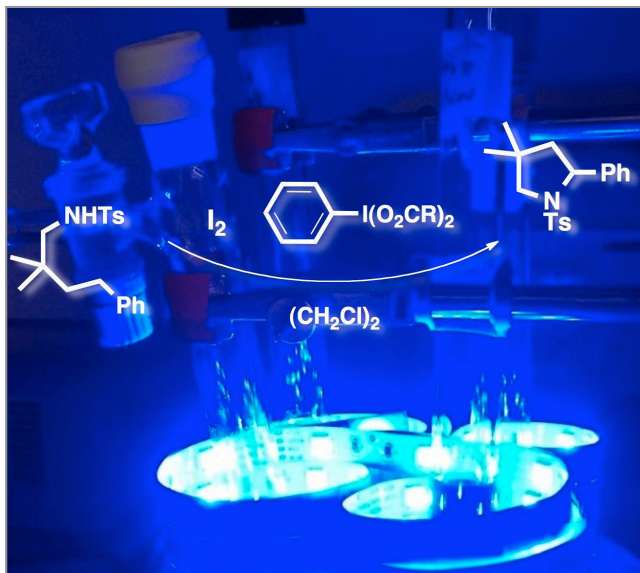


Figure 2

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

**Prof. Dr. K. Muñoz** First, a dynamic research group brings together people from many different countries to work closely together. I cannot envision any better place than Europe for doing so. I am a strong advocate of European unification and (organic) chemistry should be instrumental in promoting the benefits of this idea within the next generation of chemists. Then, organic chemistry is a timeless art and will continue to stand out for its creativity. Developing new and unexpected reactions has always been at the heart of organic chemistry. I would hope this never changes since it is one of the most exciting features of our science! To plan and execute the unknown transformation and to arrive at the target molecule is very stimulating and at the heart of any curiosity-driven research, which ultimately is what academic work has always been about. Obviously, the rules have changed a little bit over time and modern society's demands rightly require that creative organic synthesis embraces sustainability. Homogeneous molecular iodine catalysis, with its inherent economic and ecological benefits, is obviously a perfect match!

*Mattias Farnok*