

HIGHLIGHT

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Non-covalent organocatalysis in asymmetric oxidative C(sp³)-H bond functionalization – broadening C–H bond coupling reactions

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Among the current huge development activities in C–H functionalization, asymmetric oxidative C(sp³)-H bond coupling strategies have remained underrepresented. Beyond the initial examples using chiral metal complexes, the use of organocatalysis provides a new direction for the design of new asymmetric C–H bond cross-coupling reactions. This highlight focuses on the latest advances in metal-free asymmetric oxidative C(sp³)-H bond functionalization using cooperative non-covalent organocatalysis.

C–H bond functionalization has emerged as a powerful synthetic method for the efficient and straightforward construction of C–C or C–heteroatom bonds.¹ In the last decade a large number of practical applications of this C–H coupling methodology have appeared. In this regard, oxidative C(sp³)-H

bond functionalization, such as the cross-dehydrogenative coupling (CDC) coined by Li, has attracted great interest.² This type of chemistry is conceptually very simple and easy to perform. From a mechanistic point of view, it implies an initial substrate oxidation to form a cationic intermediate (or in some cases a radical) that can then undergo a nucleophilic attack to form the new C–Nu bond (Scheme 1).^{1,2} However, one of the intrinsic selectivity issues in C–H functionalization relies on the ubiquitous presence of C–H bonds in organic molecules. Therefore, in order to attain high levels of regio- and chemoselectivity, substrates such as 1,2,3,4-tetrahydroisoquinolines (THIQ), which possess a distinct prominent easily oxidizable benzylic C–H bond alpha to a N-atom, have extensively been explored.^{1–3} Although a large variety of nucleophiles have already been enrolled as reaction partners, there is still a limited number of effective and synthetically valuable enantioselective oxidative C(sp³)-H bond functionalization processes.⁴ In the earlier examples, a Cu–metal catalyst was used in combination with a chiral ligand, such as BOX or PyBOX, providing moderate to good enantioselectivities.^{5,6} On

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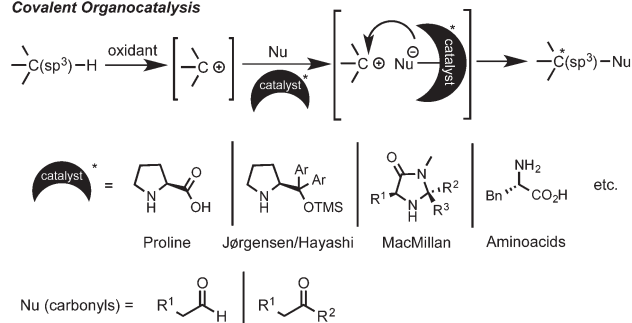


Olga García Mancheño

Olga García Mancheño received her PhD in 2005 from the Universidad Autónoma de Madrid under the supervision of Prof. Juan C. Carretero. During her PhD she carried out two–three month research-stays with Prof. Manfred T. Reetz (Max-Planck-Institut für Kohlenforschung) and Prof. Karl Anker Jørgensen (University of Aarhus). Next she moved to RWTH-Aachen University for her postdoctoral stay in the group of Prof. Carsten Bolm (2005–2008). At the end of 2008 she started her independent career as Assistant Professor (Habilitation, mentor: Prof. Frank Glorius) at the University of Münster. In 2013 she was appointed as Professor for Organic Chemistry at the University of Regensburg and the Straubing Center of Science for Renewable Resources. Her main research interests include the development of new synthetic methods, with a special focus on catalytic approaches, and their application in the synthesis of bioactive compounds and heterocycles.

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Covalent Organocatalysis



Scheme 1 Asymmetric covalent-organocatalysis approach.



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