Chiral-at-Ruthenium Catalyst Does the Job: Access to Enantioenriched 2-Imidazolidinones

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doped carbon catalysts are free from the N and Zn residuals because both could contribute significantly to the electrocatalytic performance. Furthermore, the synthetic approach might need further optimization to yield monodispersed topological defects. As well known, carbon materials produced even by the same method, but under different conditions, often have different structures and/or properties, including crystallinity, porosity, and conductivity that all will affect the electrocatalytic performance. It is still challenging to create specific defect structures as the effective catalytic sites while keeping other catalytic attributes in the carbon materials unchanged. Therefore, further optimization of synthetic methodologies and systematic structure characterization are needed for a better mechanistic understanding and future development of defective doped metal-free carbon catalysts with a well-defined structure, and therefore superior performance, of practical significance.


Chiral-at-Ruthenium Catalyst Does the Job: Access to Enantioenriched 2-Imidazolidinones

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Catalytic and enantioselective ring-closing C(sp3)‒H amidation of urea derivatives has been unexplored. In this issue of Chem, Meggers and co-workers address this challenge by using a chiral-at-ruthenium catalyst to obtain cyclic 2-imidazolidinones in a highly enantioselective manner. The latter can be converted to chiral vicinal diamines without appreciable loss of enantiopurity.

Catalytic asymmetric nitrene insertion into prochiral C(sp3)‒H bonds has been recognized as a powerful tool for the enantioselective construction of N-heterocycles. Among the known cyclized products resulting from these intramolecular reactions are sulfamidates, sulfonamides, carbamates, lactams, and Boc-protected amines. Absent from this list are chiral 2-imidazolidinones, which are ideally obtained via asymmetric ring-closing C(sp3)‒H amidation. 2-Imidazolidinones are prevalent in chiral auxiliaries and bioactive compounds,2, making them desirable target compounds. In addition, 2-imidazolidinones are precursors for the synthesis of chiral vicinal diamines, which are useful intermediates for the synthesis of numerous drugs, natural products, chiral catalysts, and ligands. The Meggers lab has developed chiral-at-ruthenium complexes that bear achiral ligands and employ the metal center as the locus of asymmetry.5 These ruthenium complexes proved to be effective catalysts for nitrene insertion reactions into C‒H bonds. Specifically, intramolecular C(sp3)‒H amidation of aliphatic azides6 or 2-azidoacetamides7 and C(sp3)‒H amidation of

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Dioxazolones\textsuperscript{8,9} were reported to afford the desired cyclic products with high turn-over numbers in a highly enantioselective manner.

In this issue of Chem, Meggers and co-workers further expand the applicability of chiral-at-ruthenium catalysts for enantioselective C(sp\textsuperscript{3})–H functionalization by adding urea derivatives to the library of nitrene precursors.\textsuperscript{10} Using N-benzoyloxyureas, 0.05–1.0 mol\% of the bis-trimethylsilyl functionalized catalyst, and 3 equiv of K\textsubscript{2}CO\textsubscript{3} (Scheme 1), the authors obtained various 2-imidazolidinones in high yields with excellent enantioselectivities (up to 99\% ee) under mild reaction conditions.

Specifically, they successfully demonstrated C(sp\textsuperscript{3})–H amidation of benzylic positions (R\textsuperscript{1} = aromatic or thiophene, R\textsuperscript{2} = Me) and a propargylic position (R\textsuperscript{1} = phenylethynyl). Desymmetrization of an indane-based substrate, to afford a 2-imidazolidinone with two stereocenters at the 4- and 5-positions, yielded 29\% of the desired product with 89\% ee. Similar desymmetrization of 1-benzoyloxy-1,3-diphenyl-2-propynylurea afforded a single diastereoisomer of the desired product in 93\% yield with 94\% ee. The authors note that the reaction is limited to activated methylene C(sp\textsuperscript{3})–H positions.

N-alkyl substituents at the urea precursor substrates are tolerated and afford 2-imidazolidinones in high yield and enantioselectivity for R\textsuperscript{2} = ethyl, n-butyl, isobutyl, and ethylphenyl (R\textsuperscript{1} = Ph), as was also observed for R\textsuperscript{2} = H. A benzyl substituent at the R\textsuperscript{2} position leads to a lower yield, but the enantioselectivity is high. Notably, employing an N-phenyl-substituted substrate obtained the corresponding C(sp\textsuperscript{3})–H amidated product.

The authors demonstrated the synthetic utility of the developed protocol by facile synthesis of (S)-4-phenyl-2-imidazolidinone (74\% yield, 99.6\% ee) and (R)-4-phenyl-2-imidazolidinone (72\% yield, 99.9\% ee), which are intermediates in the synthesis of the drug enantiomers levamisole and dexamisole, respectively (Scheme 1). Moreover, acid- and microwave-assisted hydrolysis of several of the thus obtained 2-imidazolidinones resulted in the formation of the corresponding bis-protonated chiral vicinal diamines without appreciable loss of enantiopurity (95\% ee). These chiral 1,2-diamines are intermediates in the
BIOORTHOGONAL CATALYSIS GOES CHIRAL

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Bioorthogonal nanofactories have emerged in the last decade to provide xenobiotic pathways that generate nonbiological substances in living environments. In this issue of Chem, Qu and co-workers incorporate asymmetric catalytic properties and chemotactic capabilities into novel nanodevices to achieve the stereo- and site-selective synthesis of the active enantiomer of ibuprofen at inflammation sites.

Achieving precisely localized delivery of a drug—i.e., supplying a therapeutically active agent only where needed—has challenged chemists, pharmacologists, and clinicians for over a century since Paul Ehrlich coined the “magic bullet” concept. In response, a myriad of nanovehicles have been developed over the years as selective drug-