

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.

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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.¹ Among the known cyclized products resulting from these intramolecular reactions are sulfamidates, sulfa-

mides, 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 com-

pounds,^{2,3} 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.⁴ 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

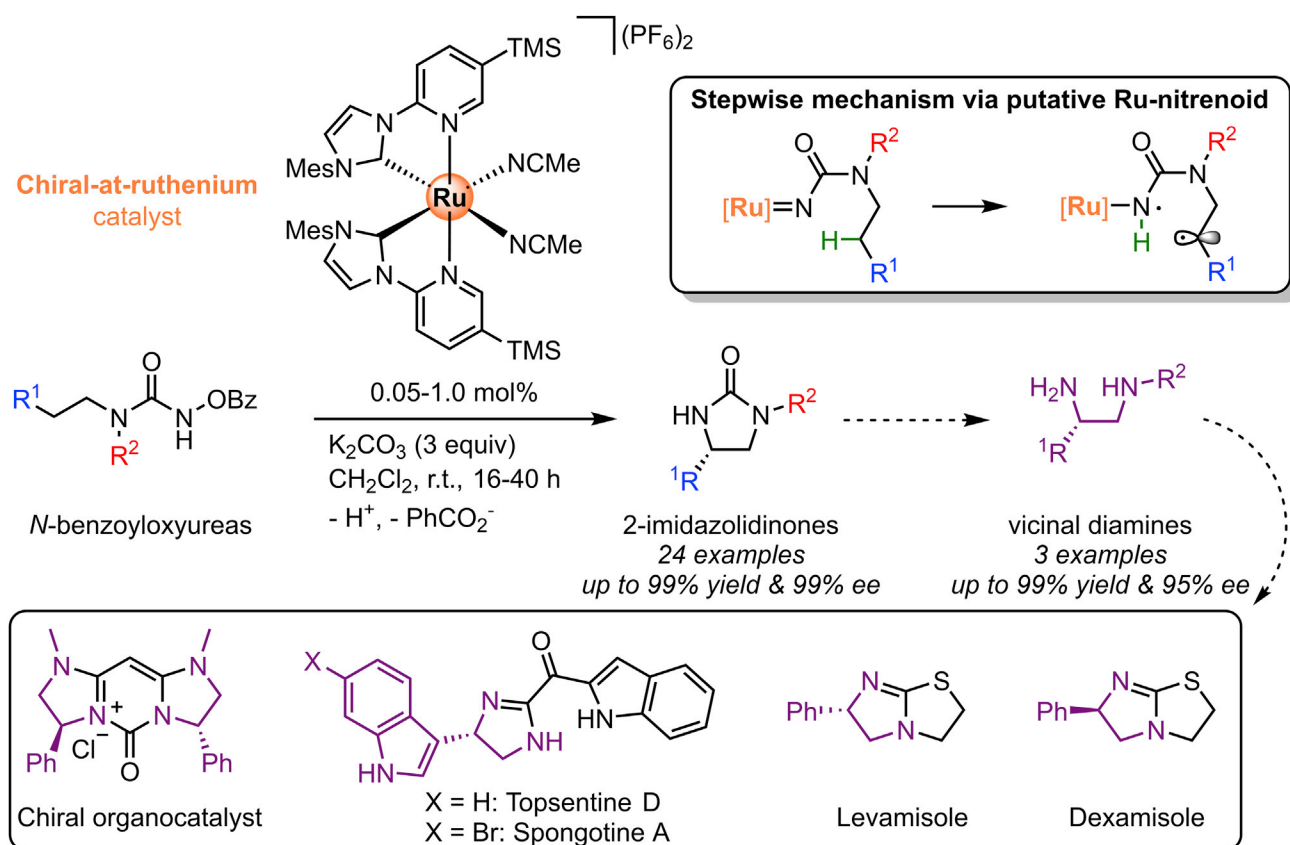
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Scheme 1. Conversion of *N*-Benzoyloxyurea Derivatives to 2-Imidazolidinones with a Chiral-at-Ruthenium Catalyst via a Putative Ru-Nitrenoid Intermediate

The cyclic ureas can be converted to vicinal diamines that serve as intermediates in the synthesis of high-valued products.

dioxazolones^{8,9} were reported to afford the desired cyclic products with high turnover 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(sp³)-N bond formation by adding urea derivatives to the library of nitrene precursors.¹⁰ Using *N*-benzoyloxyureas, 0.05–1.0 mol% of the bis-trimethylsilyl functionalized catalyst, and 3 equiv of K₂CO₃ (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(sp³)-H amidation of benzylic positions (R¹ = aromatic or thiophene,

R² = Me) and a propargylic position (R¹ = 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-propylurea 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(sp³)-H positions.

N-alkyl substituents at the urea precursor substrates are tolerated and afford 2-imidazolidinones in high yield and enantioselectivity for R² = ethyl, *n*-butyl, isobutyl, and ethylphenyl (R¹ = Ph), as was also observed for R² = H. A benzyl substituent at the R² position leads to a lower yield, but the enantioselectiv-

ity is high. Notably, employing an *N*-phenyl-substituted substrate obtained the corresponding C(sp²)-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

synthesis of topsentine D and spongatine A and are precursors to chiral organocatalysts.

A nitrene intermediate undergoing radical-type hydrogen atom transfer (HAT) reactivity was inferred by measurement of a large kinetic isotope effect ($k_H/k_D = 4.35$) via intramolecular competition between $C(sp^3)$ -H and $C(sp^3)$ -D amidation. Further indications of the formation of a carbon-centered radical were obtained by olefin isomerization studies: *N*-benzoyloxyurea with *Z*- or *E*-vinylbenzene as R^1 ($R^2 = Me$) afforded an eroded *Z/E* = 4.4:1 ratio of the former, whereas the >20:1 *E/Z* ratio from the starting material was retained with the more stable *E*-isomer.

In reactions with (*S*)-1-(benzoyl-oxy)-3-(2-phenylpropyl)urea as the substrate, stereochemistry was retained with the Δ -isomer of the catalyst, whereas the Λ -isomer led to racemization (indicating a mismatch between the Δ -catalyst and the substrate) in combination with the formation of a carbon-centered radical prone to racemization. These experiments are all consistent with the initial formation of

a putative Ru-nitrenoid (Scheme 1), formed upon base-assisted activation and deprotection of the (metal-bound) *N*-benzoyl-oxyurea substrate. Subsequent HAT from the weakest C–H bond generates a carbon-centered radical, followed by an enantioselective radical-rebound step to generate the product.

In conclusion, Meggers and co-workers have reported the first example of an enantioselective urea cyclization reaction via a nitrene-type $C(sp^3)$ -H amidation strategy with a chiral-at-ruthenium complex. The obtained cyclic compounds are valuable products in themselves and can readily be converted to desirable chiral 1,2-diamines.

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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-

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