Reductive Carboxylation of Unsaturated Hydrocarbons with CO₂

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ABSTRACT

Carbon dioxide is an attractive C₁ synthon in chemical synthesis due to its abundance, obtainability, non-toxicity, and inherent renewability. However, it has been undervalued and underutilized for the synthetic installation of carboxyl functionality because of its unreactive nature, owing to its inherent thermodynamic stability and kinetic inertness. Traditionally the carboxyl group is accessed by organic chemists through redox manipulation and protection/deprotection reactions or through the use of strong nucleophiles that have limited functional group tolerance. By fixing carbon dioxide with unsaturated organic molecules through C–C bond formation, rapid and redox-economic synthesis of carboxylic acids and their derivatives can be realized. Nevertheless, these transformations remain rare, are poorly understood, and generally limited to more energetic alkyne substrates. The Popp Research Group uses methodological and mechanistic approaches to expand the versatility and usefulness of transition metal-catalyzed reductive olefin carboxylation. Two approaches that will be discussed in this seminar are transfer hydrometallation–carboxylation and hetero(element)carboxylation. Recent mechanistic work will be presented on an iron-catalyzed variant of the former reaction class that has revealed new details, and possibly new opportunities, for this poorly understood class of reaction. The latter manifold was only recently extended by our group to include olefins (vinyl arenes) for the first time (ACS Editors’ Choice–Org. Lett. 2016, 18, 6428). The mild method uses redox-neutral copper catalysis and a single atmosphere of CO₂ to obtain boron-functionalized α-aryl carboxylic acids, including novel functionalized-NSAIDs such as bora-ibuprofen and bora-naproxen. Recent progress toward the preparation of new bora-olefin compounds, subsequent synthetic elaboration of the carbon-boron bond, and complimentary experimental/computational studies to improve our mechanistic understanding of the reaction will also be presented.