DECross - Design of New Enantioselective Decarboxylative Cross-couplings

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Carboxylic acids are widely found in commercialized chemicals and in naturally occurring compounds. Therefore, much attention is given to their catalytic activation, which over the last years resulted in the development of a variety of new synthetic methods. Among these, transition metal catalyzed decarboxylative cross-couplings (DCCs) are class of reactions that attracted significant interest in organic chemistry. These involve the activation of the substrate by removal of the carboxyl group as a molecule of CO2, and coupling of the formed metal-C bond with an electrophilic reaction partner to form a new C-C bond. However, despite the utility of this strategy, synthetic applications are limited due to the intrinsic stability and poor reactivity of carboxylic acids. In particular, this field is dominated by the DCC of benzoic acids, and aliphatic carboxylates used in transition-metal-catalyzed polar DCCs are limited to only two classes: i) α-aryl-acetates or ii) β-carbonyl acids. Moreover, enantioselective DCCs are rare, and controlling the stereochemistry at the carbanion site has never been reported. This proposal introduces an innovative activation mode for allyl and propargyl carboxylates towards novel (enantioselective) DCCs. This is enabled by a mechanistically unique decarboxylation step hat leads to the formation of allyl- and propargyl-metal intermediates capable of undergoing (enantioselective) alkylation of carbonyl compounds thus providing new C-C bond disconnections with wide applicability in organic synthesis. This proposal is set to provide new general knowledge in the catalytic activation of carboxylic acids and in their synthetic exploitation, which is a timely challenge. By unveiling a new DCC manifold and applying this to new enantioselective transformations, we aim to take DCCs to an applicative level, resulting in a significant breakthrough in the fields of transition metal catalysis and organic synthesis.

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