NICK-BOND

Nickel-catalyzed bond-forming reactions with native functional groups

Timeline | 01/2019 to 12/2022

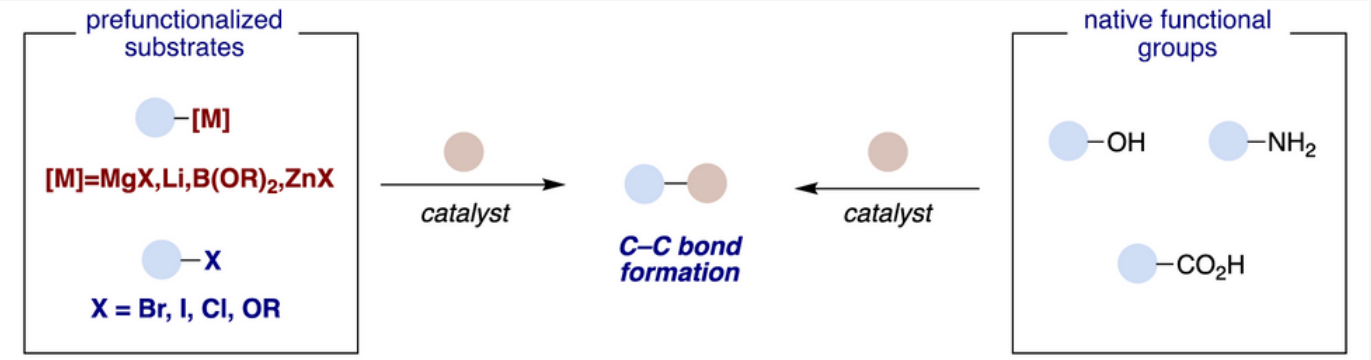
Budget | 363,000 €

ICIQ People | R. Martín Research Group

Call | Proyectos I+D - Generación Conocimiento 2018

SUMMARY

Over the last century, cross-coupling reactions have had a transformative impact in synthetic organic chemistry. Indeed, the high chemoselectivity achieved when coupling nucleophilic fragments (boronic acids, organozincs, Grignard reagents, etc) with electrophilic counterparts (typically aryl or alkyl halides) has contributed to the full adoption of these methods in both industrial and academic laboratories. Practicality and cost issues associated to these reactions, however, have spurred considerable efforts to forge CC bonds relying on naturally-occurring precursors for rapidly and reliably generating molecular complexity as a necessary goal to achieve societal, economic and environmentally objectives. This proposal aims at providing a palette of alternatives for the utilization of native carboxylic acids, alcohols, amines and/or (un)saturated hydrocarbons in many cases considered feedstock chemicals as functional handles in lieu of pregenerated organometallic or halogenated precursors for forging CC bonds with earth-abundant nickel catalysts, even in an enantioselective manner. In this manner, existing functionality could be exploited during the assembly of molecular complexity. Unlike current CH bond-functionalization technologies, this proposal will tackle the challenge of enabling functionalization at remote sp^3 CH sites of native functionalities by means of chain-walking reactions and/or photoredox catalysis with tunable, controllable and predictable siteselectivity as well as preparative utility. This project will also turn the natural abundance of carboxylic acids and amines into a strategic advantage for forging CC bonds via decarboxylative or deaminative couplings, even at remote sp^3 sites, enabling the catalytic translocation of carboxylic acids, the implementation of interchanging carbon isotope technologies, the site-selective functionalization of unactivated olefins or the design of de novo synthesis of b-amino acids, among others. **NICK-BOND** will also offer the necessary mechanistic understanding behind the utilization of native bonds as functional handles, thus fostering systematic investigations for a more prolific use of naturally-occurring molecules to streamline synthetic sequences for building up molecular complexity, an aspect of utmost relevance when accessing structural diversity for lead generation in drug discovery.



C–C bond formations via prefunctionalized or native precursors

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Reference: PGC2018-096839-B-I00