NEMESIS

Nickel-Catalyzed Regio- and Enantioselective Synthesis of Highly Substituted Allylic Amines

Timeline | 01/03/2022 to 20/06/2024

Budget | 160,932 €

ICIQ People | A. Kleij

Call | Proyectos De Colaboración Internacional 2021-2

SUMMARY

Transition metal-catalyzed asymmetric allylic alkylation is a powerful tool for the enantioselective construction of various carbon-carbon and carbonheteroatom bonds. In this context, the Tsuji-Trost reaction has been extensively applied in synthetic chemistry but with limited success towards the construction of densely substituted linear allylic amines under exquisite stereocontrol. Moreover, enantioselective preparation of branched mono-alpha and di-alpha substituted allylic amines is currently only possible using expensive, late transition metal catalysts based on rhodium, iridium and palladium whose availability will be increasingly limited and are expensive. Therefore, the development of new allylic alkylation protocols that can alleviate the use of these costly and non-sustainable metals in the preparation of these important linear and branched allylic amine compounds for pharmaceutical/fine chemical synthesis are highly desired but remain rather elusive. This project will focus on a potentially viable, though much less studied, alternative using Ni-based catalysis in the context of allylic amination reactions. Creation of a positive synergy between existing allylic chemistry and more abundant nickel catalysts offers unique potential to streamline sustainable and stereodefined synthetic routes for challenging multi-substituted allylic amine compounds. Specifically, linear allylic amines with stereodefined tri- and tetrasubstituted double bonds, and the challenging asymmetric preparation of dialpha substituted branched allylic amines are targeted. The outcome of project will offer new prospects for important scalable, cost-effective and efficient carbon-nitrogen bond formation reactions relevant to fine chemical and pharmaceutical development.

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