ABSTRACT

Chirality plays a vital role in human daily life. After the famous but tragic case regarding the Thalidomide, Food and Drug Administration (FDA) gave a guide in relation to the submission of new drug applications. As a consequence, the use of enantiomeric drugs has hugely been increased and substantial efforts have been done to develop new asymmetric syntheses of chiral drugs. In this context, the goal of this PhD project has been to design, plan and develop new organocatalytic domino methodologies for the synthesis of optically active, densely functionalized, organic molecules. The target products represent notable motifs present in many biologically active natural and non-natural substances. All the processes studied have involved a non-covalent activation of the substrates provided by chiral organic promoters. Catalysts employed are generally able to synergistically activate both the electrophile and the nucleophile through multiple hydrogen-bonding interactions and/or ion-pair formation.

In order to access chiral heterocyclic compounds, the organocatalytic cascade approaches developed allowed us to obtain enantioenriched 3-amino-substituted isoindolinones thanks to an efficient reaction of 2-formylbenzonitriles and primary amines catalyzed by multifunctional Cinchona alkaloid-derivative ammonium salts. Moreover, the use of 2-cyano-*N*-tosylbenzylidenimine led to a new class of multi-heteroatomic cyclic scaffolds containing the important *N,S*-acetal functionality, which afforded 3-thio-substituted isoindolinones by a mild acidic hydrolysis. Furthermore, during this PhD project, a useful one-pot approach to the synthesis of 2-acetylbenzonitriles was developed and these substrates were successfully used as electrophiles in a new tandem methodology for the access to 3,3-disubstituted isoindolinones under very mild conditions. Finally, another objective of this project was the synthesis of novel highly functionalized β-amino acid derivatives, which required the use of easily available Morita-Baylis-Hillman carbonates and 4-substituted isoxazolidin-5-ones.