Combined chemical and biocatalytic approach for asymmetric one-pot reactions

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Nowadays, the main goal of the industrial and academic researchers is to develop an eco-friendlier synthetic process leading to many advantages in terms of reaction times and costs. In order to achieve this purpose, the way of the atom economy implementation could be followed, and the "common" reaction procedures could be improved using green approaches, paving the way for a large-scale application of the entire process. Since the synthesis of chiral pharmaceutical compounds includes many reaction steps, making it difficult and expensive, the idea is to exploit a one-pot reaction (**Figure 1**). This protocol provides the combination in the same reaction environment of two or more different chemical reactions, whose intermediates don't need purification, thus reducing the waste of solvents, but are immediately involved in the following step as starting materials. The here proposed one-pot reaction embrace the use of a chemical catalyst and a biocatalyst, merging their different reactivity and stereoselectivity advantages. In particular, the first step consists in an asymmetric conjugate addition of aryl boronic acids to 3-azaarylpropenones containing pyridine core, using a classical rhodium complex bearing chiral diphosphine as source of chirality,[1] and the second one in an asymmetric transfer hydrogenation of aryl ketones, using an ruthenium complex coordinated to chiral diamine, or an asymmetric biocatalytic reduction of alkyl derivatives, using *Tourolopsis* genera yeast.[2] By setting up the kinetics of the first reaction, the second catalytic step can be successfully carried out affording the desired products in good enantio and diastereopure form. Moreover, there is also the possibility to immobilize both the catalysts on specific supports in order to allow the recycling of the catalysts and their use in flow systems. This combined strategy could be applied to other different types of reactions, matching chemical and biological approaches.[3,4]

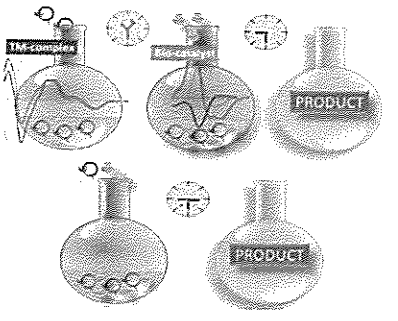

Figure 1. Temporal compartmentalization and one-pot reaction.

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