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Sommario	The importance of the synthesis of Active Pharmaceutical Ingredients (APIs) or synthetic building blocks for the construction of more complex bioactive molecules is widely recognized both in academic and industrial research. The manufacturing of drugs is an ongoing challenge for the synthetic organic chemistry, which faces several issues related to the design, the development and the optimization of synthetic processes on the basis of many aspects such as, for instance, yield, product's purity, stereoselectivity, reproducibility, environmental and economical sustainability. In the last decades the pharmaceutical research has witnessed the development of a variety of new synthetic methodologies and the implementation of innovative technologies, giving powerful tools to perform efficiently, safely and cost-effectively synthetic process. In this context, the research activity performed over the past three years of the PhD program was devoted to design and develop the synthesis of an API and molecules that can be useful as building blocks for the preparation of pharmaceutically relevant bioactive compounds. To this aim, diverse synthetic strategies were investigated, ranging from the classical organic synthesis to the traditional metal catalysed asymmetric reactions until to the use of a more innovative enabling technology that is the flow chemistry. The present thesis is divided

	into three main sections, according to these different organic synthetic methodologies. 1) Non-infringing synthesis of an Active Pharmaceutical Ingredient: Obeticholic acid. Obeticholic acid (6-ECDA) is a bile acid derivative which was discovered to be the most potent agonist of the Farnesoid X Receptor (FXR), playing a significant role in a broad range of physiological processes. The synthesis of the 6-ECDA has been object of an intense research activity as confirmed by the several patents and publications reported in the literature. In this work, a new synthesis of obeticholic acid was investigated in collaboration with the pharmaceutical company Dipharma Francis srl, with the aim of developing a new chemical process for the industrial production of obeticholic acid, without infringing the existing patented procedures in this field. In this work, all the investigated synthetic routes start from the hyodeoxycholic acid (HDCA), in place of the currently used chenodeoxycholic acid (CDCA). HDCA is a naturally occurring compound, easily extracted from the hog bile, and it could be available on a large scale more than chenodeoxycholic acid, which is widely employed in several industrial processes. In particular, two main synthetic pathways were investigated: the first one led to the final obeticholic acid and all the experimental details are included in a PCT application; whereas, the second investigated route allowed to obtain an useful intermediate for the investigation of an alternative synthesis of the obeticholic acid. 2) Synthesis of optically active biaryl compounds via asymmetric Suzuki-Miyaura cross-coupling using binaphthyl diamidophosphites as chiral ligands. The asymmetric Suzuki-Miyaura cross coupling reaction represents an efficient and powerful method to obtain axially chiral biaryl compounds, whose structural motif is present in several bioactive natural products and chiral auxiliaries. In this research activity, new chiral binaphthyl diamidophosphites derived from deoxycholic acid were synthesized and used as ligands for the preparation of mononuclear Pd(II) complexes. These latter were employed as catalysts in the asymmetric Suzuki-Miyaura cross-coupling of arylboronic acids with aryl bromides, obtaining the final biaryl compounds in moderate to excellent yields and ees up to 70 %. 3) Flow synthesis of Cyclobutanones via [2+2] cycloaddition of keteniminium salts and ethylene gas. Cyclobutanones represent valuable synthetic intermediates that can be used as building blocks for the preparation of bioactive molecules and drugs. In this work, the continuous flow preparation of 2-substituted cyclobutanones, involving [2+2] cycloaddition reaction of keteniminium species with the ethylene gas, was developed. In this way, the benefits of this enabling technologies in tackling issues associated with the use of a gaseous reagent were investigated. This research project was carried out in the laboratories of the Innovative Technology Centre, Department of Chemistry, University of Cambridge (UK), under the supervision of Prof. Steven V. Ley. The process for making 2-substitued cyclobutanones was realized by using a standard flow system equipped in line with a tube-in-tube reactor to control the introduction of the ethylene gas. This approach used rapid and mild reaction conditions to access a diverse array of 2-substituted cyclobutanones with good to excellent yield, alongside a good level of functional group tolerance.
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