Università degli Studi di Salerno

Dipartimento di Chimica e Biologia "A. Zambelli"

Ph. D. Course in Chemistry - XXXII Cycle

Abstract

New perspectives in phase transfer catalysis

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Abstract

The increasing demand for the stereoselective synthesis of bioactive compounds in both industrial and academic research has led to the rapid development of a variety of diastereo- and enantio-selective processes using phase transfer catalysis conditions. Because of its advantages, such as mild reaction conditions, simple procedures, scalability, use of inexpensive and recyclable catalysts, high selectivity and yields, phase transfer catalysis (PTC) is considered a green alternative to many homogeneous techniques. Therefore, this catalytic strategy has found widespread application in organic synthesis for the construction of several natural and unnatural compounds.

In this regard, this research project has been mainly aimed at the design and development of new stereoselective methodologies under mild phase transfer catalysis conditions for the synthesis of novel potentially bioactive products.

In the first part of the thesis, the well-known cation-binding catalytic properties of crown ethers have been further explored in previously unreported arylogous Michael additions of weakly activated and unactivated phthalides, achieving new products with high stereoselectivity and yields by using inexpensive achiral catalysts and mild reaction conditions. Phthalides attracted our interests because of their large diffusion in natural sources, their broad range of biological activities, such as anti-inflammatory and anti-bacterial properties, and the consequent extensive use in medicinal chemistry, but also for their usefulness in organic synthesis as versatile building blocks.

Next, the synthesis of enantioenriched novel products catalyzed by chiral quaternary ammonium salts has been investigated. The commercial availability, high efficiency and broad applicability of these catalysts make them ideal candidates for the discovery of new asymmetric phase-transfer transformations. In this context, the first asymmetric alkylation of 3-carboxylic-*t*-Bu-ester phthalides

has been developed, giving easy access to a novel class of potentially useful enantioenriched compounds.

Moreover, during my stay in the laboratories of Prof. Josè Alemán, at the Universidad Autonoma de Madrid, the asymmetric introduction of the SCF_3 group at C-4 position of both azlactone and isoxazolidin-5-one substrates has been developed, affording novel enantioenriched thiofluorinated compounds with high enantiocontrol of the newly generated quaternary chiral centers. The first example of enantioselective synthesis of a valuable α-SCF_3-$\beta^{2,2}$-amino acid has been also described. Knowing the attractive features of fluorine-containing molecules, relevant applications of these new chiral thiofluorinated products in the pharmaceutical and medicinal field could be envisaged.