

Titolo: Reazioni di carbonilazione catalizzate da complessi aril α -diiminici di Palladio (II): sintesi di prodotti ad alto valore aggiunto e calcoli DFT.

Title: Carbonylation reactions catalyzed by aryl α -diimine/Palladium(II) complexes: synthesis of high added value products and DFT calculations.

Research Project

This project combines organometallic catalysis with computational chemistry, in order to develop efficient catalytic systems, capable of promoting carbonylation reactions of a wide range of unsaturated substrates, for the synthesis of products valuable both for material sciences and for the pharmaceutical industry.

Carbonylations are very useful reactions due to their ability to convert low cost molecules into highly valuable carbonylated compounds, such as lactones, esters and ketones. In particular, in the bis-alkoxycarbonylation reaction of olefins, a formal double addition of a carboxylate group occurs to form succinic acid esters derivatives, which find application in various industrial fields and are important building blocks in medicinal chemistry. A methodology for the oxidative bis-alkoxycarbonylation of low reactive alkenes, such as 1,2-disubstituted^[1] and electron-deficient olefins,^[2] yielding variously substituted succinic diesters, has recently been developed. The reaction proceeds under mild conditions (20°C and 4 bar of CO pressure), using an aryl α -diimine/palladium(II) catalyst, *p*-benzoquinone (BQ) as an oxidant and an alcohol that acts both as a solvent and as a nucleophile. Recent DFT studies have disclosed some interesting aspects regarding this type of reaction, highlighting some still unclear aspects of the catalytic cycle.^[3]

The present research project foresees the acquisition of experimental data on palladium-catalyzed bis-alkoxycarbonylation reactions of alkenes and their interpretation through computational studies, in order to improve the efficiency and selectivity of the studied processes.

Initially, in order to make this type of carbonylations more efficient, appropriate modifications will be made to the ligand. In particular, non-symmetrically substituted aryl- α -diimine and aryl-iminopyridine ligands will be synthesized and tested. The best catalytic system will be then applied to the bis-alkoxycarbonylation of olefins bearing an electron-donating group in the allylic position (e.g. allyl acetates or *N*-allyl amides). In addition, in order to widen the range of the obtainable products, the reaction will be extended to olefins containing an internal double bond, such as unsaturated fatty acid methyl esters, and differently hindered alcohols, including diols, will be used as nucleophiles. An asymmetric version of the oxidative bis-alkoxycarbonylation of olefins will be investigated using optically active α -diimine ligands.

Based on the acquired information, closely related processes will also be explored. Therefore, the possibility of selectively obtaining mono-carbonylated products will be investigated and copolymerization reactions of carbon monoxide with conjugated polar alkenes (e.g. acrylic esters and acrylic amides) will be studied.

The catalytic cycles of the above described reactions will be examined using computational chemistry tools, with particular interest for the involved intermediates and for the transition states. The outcome of these studies will be used to improve efficiency and selectivity of the carbonylation processes and to address the experimental work. Density Functional Theory (DFT) methods will be utilized to investigate new possible synthetic routes, such as mono-carbonylation and copolymerization reactions. Moreover some attempts will be made to isolate and characterize the intermediates envisaged by the calculations.

^[1] D. Olivieri, F. Fini, R. Mazzoni, S. Zacchini, N. Della Ca', G. Spadoni, B. Gabriele, R. Mancuso, V. Zanotti, C. Carfagna *Adv. Synth. Catal.* **2018**, *360*, 3425.

^[2] D. Olivieri, R. Tarroni, N. Della Ca', R. Mancuso, B. Gabriele, G. Spadoni, C. Carfagna, *Adv. Synth. Catal.* **2020**, *362*, 533.

^[3] C. Mealli, G. Manca, R. Tarroni, D. Olivieri, C. Carfagna, *Organometallics* **2020**, *39*, 1059.

Work Plan

The planned research activity is in the field of organometallic chemistry, homogeneous catalysis and computational chemistry. The following points will be investigated:

- Synthesis, characterization and application in Pd-catalyzed carbonylation reactions of the following ligands: non-symmetrically substituted aryl α -diimines, aryl-iminopyridines and optically active nitrogen ligands of α -diimine type.
- Development of bis-alkoxycarbonylation reactions using, as substrates, olefins bearing an electron-donating group in the allylic position and, as nucleophiles, variously hindered alcohols or diols.
- Study of mono-alkoxycarbonylation reactions.
- Development of electron-deficient olefin/carbon monoxide copolymerizations.
- Study of the catalytic cycles through DFT calculations.
- Mechanistic and computational investigations to develop new synthetic routes in the field of carbonylations.
- *Ad hoc* synthesis and characterization of the possible key intermediates, envisaged by the calculations.

The research activity will be carried out at the Rimini Campus of the University of Bologna and in part at the Department of Biomolecular Sciences of the University of Urbino "Carlo Bo".

The proposed research will be carried out in close collaboration with Prof. Carla Carfagna.