

## **Abstract**

In this doctoral work, we developed transition metal-catalyzed transformations of organic molecules using affordable transition metals such as copper, ruthenium, and nickel. These methods introduce new approaches in synthetic chemistry, and their application to biomolecules enables the modification of their properties. We optimized copper-catalyzed cycloaddition of alkynes and hydrazoic acid ( $\text{HN}_3$ ) to meet 'click' reaction conditions, extending the CuAAC reaction to the use of  $\text{HN}_3$ . We demonstrated the developed reaction on various substrates and isolated the products – *NH*-triazoles – with high yields. This reaction was used to prepare synthetically important precursors and applied in the final synthesis step of a losartan analogue. The reaction also achieved a high conversion rate on peptide substrates. We also incorporated *NH*-triazole into peptides using solid-phase peptide synthesis with the amino acid *L*-azahistidine and purified the synthesized peptides with advanced chromatographic techniques. We applied the CuAAC reaction with  $\text{HN}_3$  to four proteins, into which an alkyne handle was previously introduced using *N*-hydroxysuccinimide esters (NHS). Insulin modified with *NH*-triazoles showed significantly increased thermal stability while maintaining its cellular activity even after prolonged exposure to high temperatures. We developed a series of NHS-triazole reagents that allow easy attachment of *NH*-triazole to any protein. Additionally, we developed two new ruthenium-catalyzed hydrogenation transformations based on transfer hydrogenation: hydrogenation of alkynes to alkanes and partial hydrogenation of disubstituted alkynes to alkenes, proceeding in tandem with Sonogashira cross-coupling. We demonstrated these reactions on various substrates and prepared a pharmaceutically important compound – combretastatin A4. We developed a homogeneous nickel-catalyzed hydroarylation reaction of styrenes and demonstrated it on a series of substrates. Through mechanistic experiments, we proposed the reaction mechanism, confirmed it with DFT calculations, and demonstrated a computational model for predicting suitable catalysts. We also explored heterogeneous catalysis, using a nickel catalyst based on a zeolitic imidazolate framework for Suzuki coupling.