

# **Iron or Copper?**

## **– Method Development and Mechanistic Studies on Cross-Coupling Reactions**

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## **Abstract**

The area of catalysis has had an immeasurable impact on modern society. This has been acknowledged through several Nobel prizes during the 20th century ranging from Haber (1918) for the synthesis of ammonia to Richard F. Heck, Ei-ichi Negishi, and Akira Suzuki (2010) for palladium-catalyzed cross-coupling reactions.

The development of efficient cross-coupling reactions has made this transformation a vital instrument in the method library of organic synthesis. Today, cross-coupling reactions are widely used in industrial applications in areas such as fine chemical production and pharmaceutical industry. With increasing demands on environmentally friendly and cheaper alternatives to the commonly used palladium and nickel catalysts several alternative metals have been evaluated. Among these, both iron and copper have experienced a revival during the past two decades.

The iron-catalyzed cross-coupling reaction has proved successful for a range of transformations but the mechanistic picture behind these reactions is still not entirely comprehensive. Several important mechanistic features for this reaction are presented in this thesis based on experimental studies such as titration, kinetic, and competitive Hammett study. Several of these experimental results are supported by computational studies done by Dr. Kleimark.

In the pursuit of finding alternative catalysts for known transformations one has to consider the presence of potential trace-metal contaminants. The case presented in this thesis concerns the “iron” catalyzed C-N cross-coupling reaction which turned out to be catalyzed by traces of copper present in the commercially available iron source.

The discovery that many copper-catalyzed cross-coupling reactions could be run with much lower catalytic loadings than previously reported further strengthened the role of copper as a viable catalyst in cross-coupling reactions. Method development, kinetic studies and ligand synthesis for sub-mol% copper-catalyzed transformations are presented in this thesis.

**Keywords:** iron, copper, transition-metal, cross-coupling, reaction mechanism, kinetic investigation, Hammett study, sustainable catalysis, trace-metal, mass-transfer, ligand development, ligand scope.

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