

Abstract

Index No: 12/21/Chem/27

Thesis Title: Copper (II) Catalyzed C-C and C-O Bond Formation in Organic Synthesis and Their Applications

The main aim of the research work is functionalization of C-H bond in presence of cheap and earth abundant copper catalyst under mild reaction conditions. Copper catalysts are indeed ubiquitous catalysts in organic transformations due to their versatile oxidation states and their ability to participate in a broad range of reactions *via* both radical and two-electron transfer mechanisms. Copper's ability to access a range of oxidation states, typically from 0 to +3, makes it highly adaptable in catalysis. The work presented in this study reports the C-H bond activation of various organic derivatives using copper as catalyst under an oxidative environment by CDC mechanism to construct complex organic molecules and their applications in various fields.

In **first work**, we report for the first time that the quinoline-based NNN-pincer Cu(II) complex acts as an air stable superior catalyst for the oxidative cross-coupling of the allyl C(sp³)-H bond with an acid derivatives for the construction of C-O bond at ambient temperature in a homogeneous system. The synthesized catalyst **1**, showed excellent catalytic activity for the oxidative esterification of allylic C(sp³)-H bonds at 40 °C within a very short time (1 h) using only 1 mol% of the catalyst. A wide variety of aromatic allylic esters were synthesized in moderate to good yields, which could be extended to aliphatic allyl esters as well.

Further, we have developed a methodology for C-O bond formation in **second work** at slightly elevated temperature. In this context, we have developed a novel benzothiazole appended 2,6-di picolinamide-based Cu(II) complex which acts as a catalyst for the formation of carbamates *via* the cross-coupling reaction of various 2-carbonyl substituted phenolic derivatives or 1,3-diketo derivatives with N,N-disubstituted formamides. A wide range of aromatic carbamates was synthesized using copper complex in good/excellent yield with decent functional group tolerance under mild conditions. Control experiments suggest that the reaction proceeds *via* the radical

mechanism, and the formation of radical-mediated intermediates was confirmed by the gas chromatography (GC), GCMS and HRMS. The use of low cost and environmentally benign catalysts in mild conditions along with the tolerance of a wide range of functional groups makes this an easy synthetic approach for the development of carbamates.

In **third work**, we report the Cu(II) catalyzed synthesis of β -disubstituted ketones from styrene *via* oxo-alkylation with unactivated cycloalkanes as the alkylating agent in presence of tert-butylhydroperoxide (TBHP) and 1-methylimidazole as oxidant and base respectively. β -disubstituted ketones are known to be synthesized by using either expensive Ru/Ir complexes, or low-cost metal complexes (e. g., Fe, Mn) with activated species like aldehyde, acid, alcohol, or phthalimide derivatives as the alkylating agent, however, use of unactivated cycloalkanes directly as the alkylating agent remains challenging. A wide range of aliphatic C–H substrates as well as various olefinic arenes and heteroarene are well-tolerated in this method. Furthermore, various controlled experiments such as kinetic isotope effect study, Hammett analysis and theoretical calculations (DFT) enable us to gain deeper insight of mechanistic intricacies of this new simple and atom-economic methodology.

The work in **Chapter 5** does not include any catalysis work rather, in this work we have developed a unique probe *via* Cu(II) catalyzed Glaser-Hay coupling. The designed probe is capable of detecting dual metal ions *via* different binding sites and different mechanisms within a single molecular scaffold. On account of this, two pyridine-derived scaffolds, **5** and **7**, containing identical molecular cores but different appendages, *viz.*, terminal alkyne (**5**) and internally 1,3-conjugated alkyne units (**7**), are successfully synthesized. Alkyne is a versatile functional group in organic chemistry, and can undergo a wide variety of reactions and interactions. Both compounds are subjected to metal ion sensing at the molecular level and are found to bind Cu²⁺ and Hg²⁺ ions with different functionalities. Compounds **5** and **7** interact with Cu²⁺ by the pyridine N and the two adjacent amide N's in a tripodal fashion, whereas they interact with Hg²⁺ by their respective open-end and closed-end alkyne units. Both experimental studies and theoretical (DFT) calculations have converged on the result that terminal alkynes cannot function as a chemosensor for Hg²⁺ ions, although they can respond by functional group transformation, whereas cyclic internally

conjugated alkynes can perform as potential Hg^{2+} sensors. The combination of Cu^{2+} and Hg^{2+} ions has been used to generate a molecular system exhibiting the OR logic operation. This creates an avenue for differential recognition of multiple heavy metal ions simultaneously with similar molecular motifs.

AThkur. 15/05/24

Signature of the Supervisor (date with official seal)

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