Introduction

Transition metals play a crucial role in advancing modern organic synthesis, as they enable chemists to create complex compounds with greater precision, efficiency, and selectivity. These metals play key roles in a variety of reactions as catalysts, intermediates, and constituents, enabling the creation of new chemical bonds and the conversion of low-value starting materials into highly valuable end products. The role of transition metals in organic chemistry, especially palladium and copper, is extremely important. These metals are essential to the growth and development of contemporary organic synthesis because they help chemists produce complicated compounds more precisely, efficiently, and selectively. Transition metals play key roles in a variety of reactions as catalysts, intermediates, and constituents, enabling the creation of new chemical bonds and the conversion of low-value starting materials into highly valuable end products. We will examine the special qualities and reactivity of palladium and copper in this in-depth analysis of their significance. By doing so, we will throw light on their crucial roles in a variety of organic transformations and demonstrate the enormous influence they have had on the study of chemistry.

Palladium, a *4d* transition metal, has a remarkable versatility that has revolutionised organic synthesis. Due to its special qualities, it is the perfect catalyst for a variety of reactions. Most notably, it is ideal for cross-coupling reactions, such as Heck, Stille, and Suzuki-Miyaura reactions, which are crucial for the formation of carbon-carbon and carbon-heteroatom bonds needed to produce advanced materials, agrochemicals, and pharmaceuticals. For example, the Heck reaction allows for the direct arylation of alkenes, which are important structural motifs in medicines and natural goods, which simplifies the synthesis of biaryl compounds. Another example of palladium's versatility is the Suzuki-Miyaura reaction, which makes it easier to couple aryl halides with organoboron compounds. This coupling is essential for the synthesis of drug candidates, dyes, and materials for organic electronics.

Palladium plays an important role in hydrogenation reactions as well. It acts as a catalyst for the selective addition of hydrogen to unsaturated compounds, which has a big impact on the petrochemical and pharmaceutical sectors. Furthermore, by following the guidelines of green chemistry, palladium-catalysed carbonylation contributes to sustainable chemical synthesis and is essential in the production of carboxylic acids, esters, and amides, which are vital in the pharmaceutical and agrochemical industries. In conclusion, palladium is essential to current organic synthesis because of its versatility and distinct reactivity, which allow for the accurate and effective synthesis of important compounds and open the door to more inventive and sustainable organic chemistry in the future.

In addition to palladium, copper is another metal that has become essential for the organic chemist. Copper's catalytic versatility is closely tied to its ability to cycle between oxidation states, primarily Cu(I) and Cu(II), which facilitates a wide range of organic transformations. The redox potential of copper enables it to act as both an electron donor and acceptor, making it an adaptable catalyst in various reaction mechanisms. For example, in the Chan–Lam coupling, copper undergoes a redox cycle that allows efficient bond formation between carbon and heteroatoms (such as nitrogen or oxygen). Copper's standard reduction potentials— +0.52 V for Cu(II)/Cu(I) and +0.34 V for Cu(II)/Cu(0)—highlight its moderate oxidising and reducing power, which is well-suited for catalysing these selective transformations without requiring extreme conditions. This redox flexibility is crucial in reactions like the Glaser and Ullmann couplings, where copper cycles between oxidation states to promote C–C bond formation

Herein, we study the catalytic activity of palladium and copper in C –C and C–heteroatom bond formations towards the synthesis of biphenyls, indoles and in the N-H functionalisations of imidazoles and benzimidazoles.

2. Objectives

Keeping in mind the catalytic activity of Palladium and Copper in organic transformations, following objectives are proposed for the thesis:

- Utilisation of Pd(II) salt in the directing group (-COOH) assisted *ortho*-C-H arylation reaction. Ligand directing group assisted C-H arylation helps in arylation at positions that are conventionally hard to achieve.
- Utilisation of supported palladium catalysis in C-C and C-O bond formation reactions. Supported catalysis involving palladium centers provides efficient ways to form C-C and C-O bonds and gives heterogeneity.

- Utilisation of Pd(II) salt in intramolecular Heck cyclisation for the synthesis of indoles. Intramolecular Heck reaction is a powerful tool for making C-C bonds and synthesising molecular systems under Pd(II) catalysis due to its wide functional group tolerance.
- Utilisation of copper nanocatalysis for the formation of C-N bonds. Among the various C-N bond formation reactions, Chan-Lam cross-coupling strategy is the most sought-after process on account of its versatility and wide tolerance of functional groups.

3. The Thesis

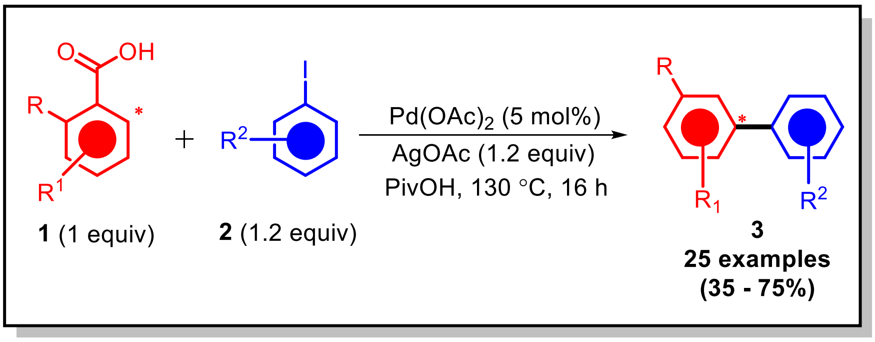
The thesis consists of six chapters. **Chapter 1** gives a general introduction to the thesis and discusses about the utility of transition metals, mainly palladium and copper in organic and organometallic chemistry. **Chapters 2** and **3** focus on the catalytic activity of palladium (II) salt and palladium (0) nanomaterial in specific organic transformations, while **chapter 4** explores the *in-situ* generation of palladium (0) nanoparticles from a palladium (II) salt and their impact on organic transformations. In **chapter 2**, a palladium (II)-catalysed o-arylation-decarboxylation cascade involving *ortho'*-substituted benzoic acids is examined to produce *meta*-substituted biphenyls. In **chapter 3**, divided into **chapters 3a** and **3b** the utilisation of lignocellulose-supported palladium nanoparticles is investigated for the Suzuki-Miyaura cross-coupling of aryl diazonium tetrafluoroborates with aryl boronic acids (**chapter 3a**) and de-nitrative *O*-arylation of phenols with nitroarenes (**chapter 3b**). **Chapter 4** delves into the use of a palladium (II) salt for the *in-situ* generation of nanoparticles, which are subsequently employed in the Heck-type cyclisation of 3-(2-iodophenyl)amino)acrylate esters and *N*-allyl-2-iodoanilines (chapter 4a) and in the intramolecular Heck cyclisation of 3-((2-bromophenyl)amino)acrylate esters (**chapter 4b**). **Chapter 5** on the other hand is concerned with the application of a copper-based nanomaterial for the *N*-arylation of imidazoles and benzimidazoles with arylboronic acids. Finally, **chapter 6** discusses about the key findings of the thesis and future aspects as well as the potential avenues in expanding the present research.

Chapter 1. General Introduction

This chapter discusses the significance of transition metals in general and palladium and copper in particular in C-C and C-heteroatom bond formation reactions. Various processes concerned with C-C and C-heteroatom bond formations with the use of Pd/Cu-salts and nanoparticles have been shown along with discussions on their merits and demerits. The objectives of the thesis are outlined towards the end.

Chapter 2. Palladium (II) Catalysed Access to *meta*–Substituted Biphenyls *via* Carboxylic acid Directed *ortho*–Arylation–Decarboxylation Cascade

Herein, a Pd(II) catalysed protocol for the synthesis of *meta*- substituted biphenyls has been devised. In this protocol, a C6-arylation-decarboxylation cascade involving C2-substituted benzoic acids (1) with aryl iodides (2) in the presence of Pd(II) acetate is observed. The utilisation of a bulky protic acid solvent prevents the major side product (solvent arylation). The treatment of 1 equivalent of the benzoic acid with 1.2 equivalents of the aryl iodide in the presence of 5 mol% of $Pd(OAc)_2$ and 3 equivalents of Pivalic acid as the reaction medium at 130 °C affords the required biphenyl product (3) efficiently. A silver (I) salt (silver (I) acetate) is also required in the reaction for the completion of the catalytic cycle. Control experiments suggest the initial arylation of the aromatic acid at the C6 position and subsequent decarboxylation (**Scheme 1**). The plausible mechanism of the reaction suggests an *ortho*–carboxylate directed C-H activation by Pd(II) to form a five membered metallacycle which is followed by aryl addition and aryl transfer followed by decarboxylation. The computational studies of the reaction are also suggestive of a plausible C6 arylation-decarboxylation cascade.



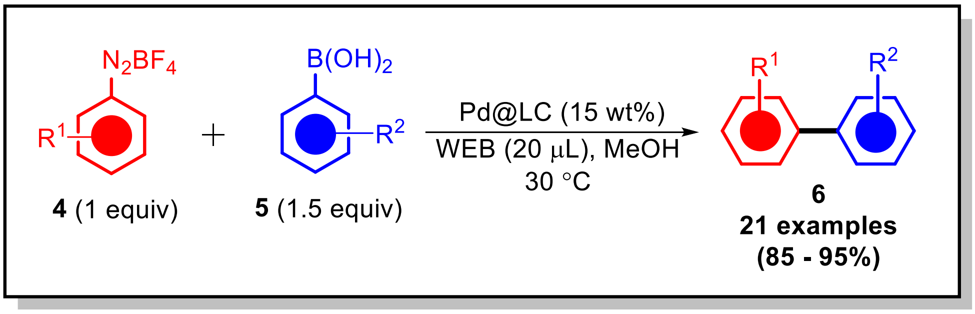
Scheme 1. Synthesis of *meta*-substituted biphenyls from benzoic acids and iodoarenes

Chapter 3. Utilising Palladium (0)-Supported Lignocellulosic Biomass Catalyst for C-C and C-O Bond Formations

This chapter delves into the catalytic ability of palladium nanoparticles supported over lignocellulose obtained from pomegranate peels in the formation of C-C bonds in a Suzuki-Miyaura type cross-coupling of aryl diazonium salts with Arylboronic acids and in the construction of C-O bonds in the de-nitrative arylation of phenols with nitroarenes to form diaryl ethers. This has been divided into two sub-chapters, **3a** and **3b**.

Chapter 3a. Utilising Palladium (0)-Supported Lignocellulosic Biomass Catalyst for Suzuki-Miyaura Type Cross-Coupling of Aryl Diazonium Salts with Arylboronic acids

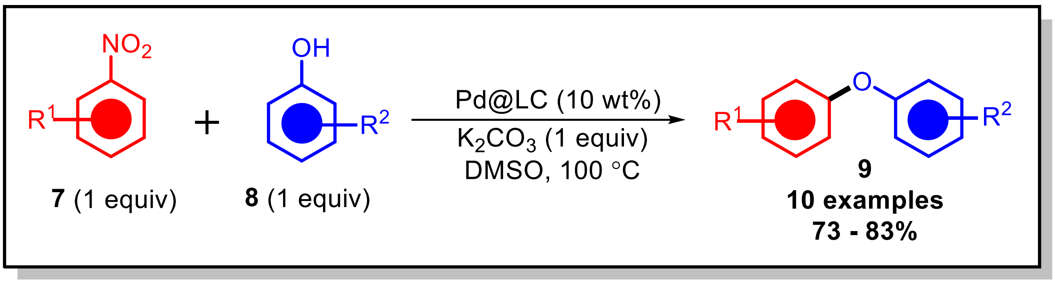
In this chapter, lignocellulose derived from discarded pomegranate peels [10], has been employed as an environmentally friendly, carbon-neutral resource, serving as a support material for palladium nanoparticles. This was achieved through a straightforward aqueous extraction method without altering its natural morphology and was characterised through TEM analysis. The system effectively catalysed the Suzuki-Miyaura cross-coupling of aryl diazonium tetrafluoroborates with arylboronic acids and was able to be reused for three cycles due to its heterogeneity. Only a 15 wt% of the catalyst was seen to be optimal in the reaction of 1 equivalent of the aryl diazonium salt (4) with 1.5 equivalents of the aryl boronic acid (5) at 30 °C. An additive in the form of WEB (water extract of banana peel ash) was seen to enhance the reaction by activating the boronic acid. The developed methodology results in the formation of biphenyls (6) with good yields. The heterogeneity of the catalyst allows its usage up to 3 catalytic cycles (**Scheme 2**).



Scheme 2. Suzuki-Miyaura cross-coupling of aryl diazonium tetrafluoroborates with aryl boronic acid catalysed by lignocellulose supported palladium nanocatalyst

Chapter 3b. Utilising Palladium (0)-Supported Lignocellulosic Biomass Catalyst for De-nitrative Cross-Coupling of Nitroarenes with Phenols

In this chapter, the palladium nanocatalyst reported in chapter 3a, has been utilised for the de-nitrative Ullmann type cross-coupling of nitroarenes (7) with phenols (8) for the synthesis of diaryl ethers (9). The reaction tolerates electron withdrawing group activated nitroarenes. Hot filtration test shows catalyst leaching into the reaction medium (**Scheme 3).**



Scheme 3. *O*-arylation of phenols with nitroarenes using Pd@LC nanocatalyst

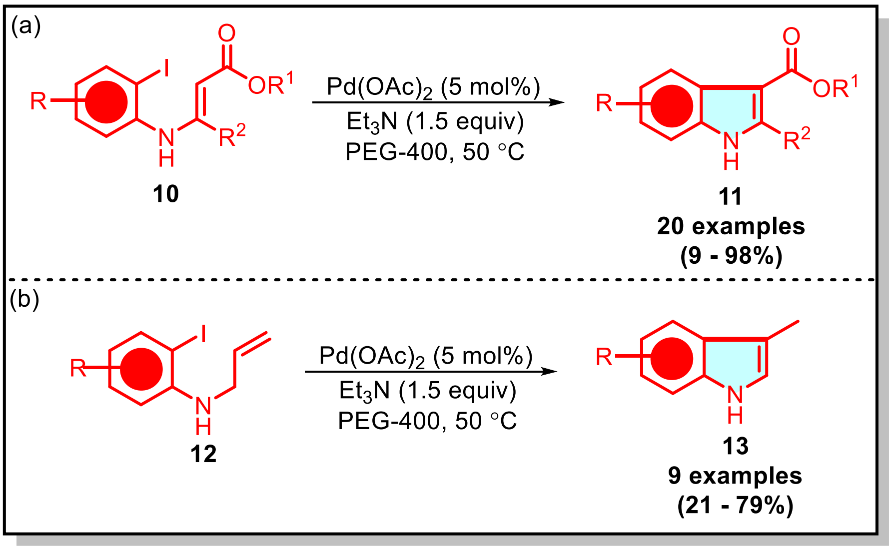
Chapter 4. Palladium (II)–PEG System for the Efficient Synthesis of Indoles *via* Intramolecular Heck Cyclisation

In this chapter, *in-situ* generated palladium nanoparticles have been utilised as heterogeneous catalysts in the Heck and Mori-Ban type cyclisations to generate the biologically relevant indole nucleus.

Chapter 4a. *In-situ* Generated Palladium Nanoparticles Catalysed Synthesis of Indoles *via* Intramolecular Heck Cyclisation of *N*-vinyl and *N*-allyl-2-iodoanilines

In this chapter, the cyclisations of *N*-vinyl-2-iodoanilines (3-((2-iodophenyl)amino)acrylate esters, 10)) and *N*-allyl-2-iodoanilines (12) has been achieved with the utilisation of the Pd(II)/PEG-400 system. The resulting indoles (11, 13) were obtained in good to excellent yields. The PEG-400 solvent owing to its capability of acting both as a reducing agent and a stabiliser of nanoparticles, helps in the formation of catalytically active palladium nanoparticles. This makes the system heterogeneous and reusable.

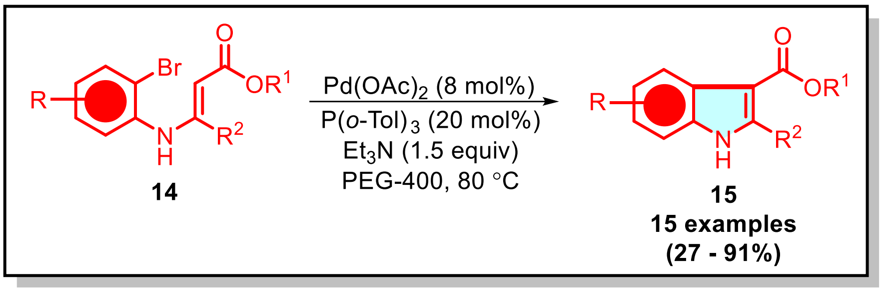
N-vinyl-2-iodoanilines (10) and *N*-allyl-2-iodoanilines (12) were prepared by the *aza*-Michael addition of 2-iodoanilines with propiolate esters and nucleophilic substitution reaction with allyl bromide respectively. Only 5 mol % of the catalyst was optimal for the cyclisation in the presence of triethyl amine (Et_3N) as base to facilitate the β-hydride elimination step (**Scheme 4**). The system has been reused to 3 catalytic cycles and has been scaled up to the gram scale. that *N, N*-diallylanilines can also be efficiently converted to generate *N*-allyl-3-methyl indoles.



Scheme 4. Cyclisation of 2-iodoaminoacrylate esters using Pd(II)/PEG-400 system to generate indoles

Chapter 4b. Palladium (II)–PEG System for the Efficient Synthesis of Indoles *via* Intramolecular Heck Cyclisation of *N*-vinyl-2-bromoarenes

Palladium (II) – PEG system also efficiently catalyses the cyclisation of *N*-vinyl-2-bromoanilines (3-((2-bromophenyl)amino)acrylate esters, 14). The attempts related to the cyclisation of 2-bromoaminoacrylate esters were seen to require an elevated catalyst amount (8 mol%) and a sigma donor ligand (P(o-Tol)$_3$, 20 mol%) owing to the higher bond energy of the aromatic sp^2-C-Br bond. The reaction also required a higher temperature of 80 °C in the presence of PEG-400 as solvent (**Scheme 5**). Under these conditions, substituted indoles (15) were furnished in good to excellent yields.

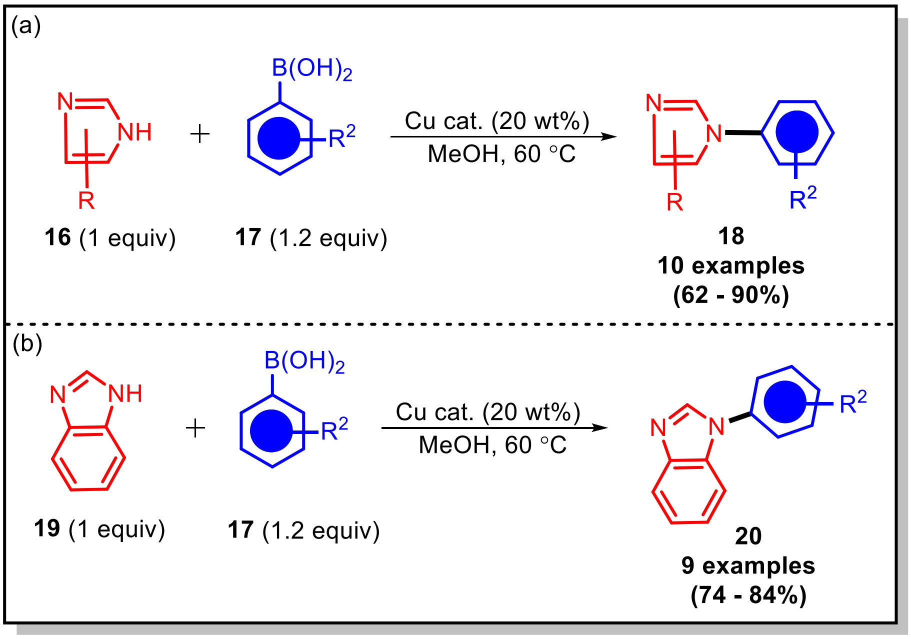


Scheme 5. Cyclisation of 2-bromoaminoacrylate esters in Pd(II)/PEG-400 system to generate indoles

Chapter 5. Biogenic Cu_2O/Cu Nanomaterial Catalysed *N*-arylation of Imidazoles and Benzimidazoles with Arylboronic acids Under External Base Free Conditions

This chapter delves into the application of household waste in the field of chemistry, a prominent area of contemporary research focused on waste reuse and valorisation. Within this context, we have harnessed discarded papaya peels to synthesise a hybrid nanomaterial comprising copper (I) oxide, which is uniformly dispersed on spherical copper nanoparticles. This hybrid copper oxide nanomaterial synthesis was achieved through an environmentally sustainable solvothermal process, involving the controlled *in-situ* formation of copper (I) oxide (Cu_2O) facilitated by waste papaya peels. Employing an *in-situ* gas phase H_2O/O_2 activation method, which entails the deposition of Cu_2O on the surface of copper nanoparticles (NPs) using an aqueous extract of papaya peel, results in the production of a biphasic Cu_2O/Cu nanomaterial. The presence of the Cu(I) phase in the material is corroborated by the appearance of a peak at 2θ (36.39°) in the powder X-ray diffraction (XRD) spectrum, corresponding to the (111) plane of Cu(I). This catalyst exhibits activity in the *N*-arylation of imidazoles and benzimidazoles with aryl boronic acids. An optimal catalyst loading of only 20 wt% is effective in the cross-coupling of aryl boronic acids with imidazoles/benzimidazoles (as shown in **Scheme 6(a)** and

(b)) in methanol as the solvent at 60 °C. The heterogeneous nature of the catalyst enables its reuse for up to three consecutive cycles.



Scheme 6. *N*-arylation of imidazoles and benzimidazoles catalysed by Cu_2O/Cu nanomaterial

Chapter 6. Conclusion and Future Scope

This chapter serves as a concise overview of the key findings from the preceding studies. Additionally, it offers insights into potential avenues for expanding and enhancing the present research.

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Keywords

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Heterogeneous

Imidazole

Indole

Lignocellulose

Nanocatalyst

Nanomaterial

Palladium

Reusability

Transition metal