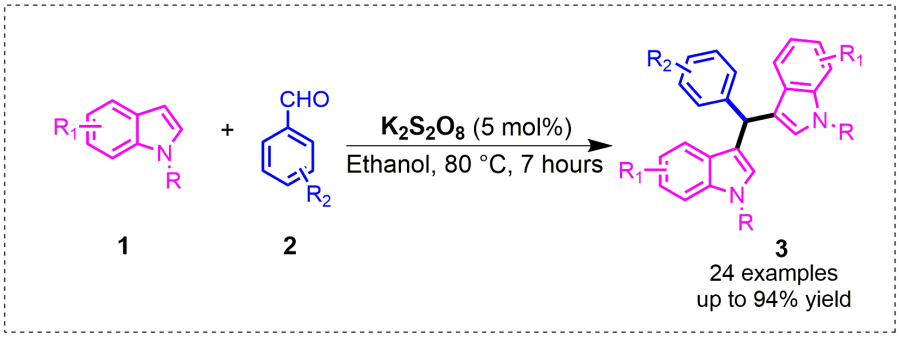
The work incorporated in the thesis illustrates a study on the strategic functionalization of indoles and oxidative coupling reactions for $C(sp^2)$-$C(sp^2)$ and $C(sp^2)$-$C(sp^3)$ bond formation under ambient conditions. The main text of the thesis has been arranged into seven chapters.

Chapter 1: Introduction

This chapter describes the literature review of functionalization of indoles and related molecules, Suzuki-Miyaura reaction with heterogeneous catalyst and C-C bond formation reaction with decarboxylative coupling of cinnamic acids. The objectives of the thesis are also outlined towards the end.

Chapter 2: Potassium peroxodisulfate catalyzed convenient synthesis of bis(indolyl)methanes *via* radical path

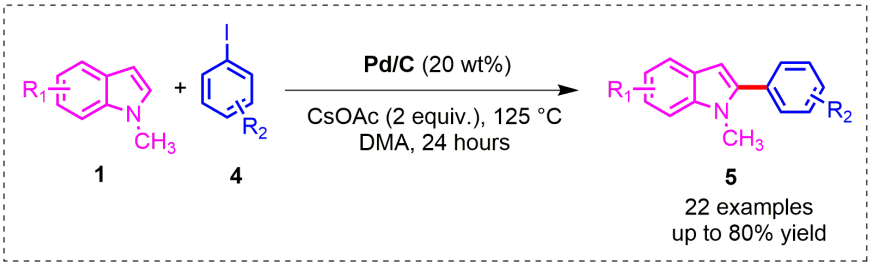
In this chapter, we discuss an alternative methodology for the synthesis of bis(indolyl)methane (BIM) by using potassium peroxodisulfate ($K_2S_2O_8$) as a catalyst under ambient conditions. Bis(indolyl)methane is a biologically active indole-containing compound having a methylene bridge between the two indole scaffolds. In our methodology, we have used different indole (**1**) and aldehyde (**2**) derivatives, and only 5 mol% of $K_2S_2O_8$ can efficiently proceed the reaction (Scheme **1**). With a cheap and an easily available laboratory reagent $K_2S_2O_8$, this protocol is applicable for both electronically and sterically varied substrates (without affecting -Br, -Cl, -NO_2, -OCH_3, and -OH groups) with a good to excellent yield (up to 94%) of bis(indolyl)methane (**3**) derivatives under air. Since $K_2S_2O_8$ is known as the free radical initiator, and therefore to prove the possible involvement of the free radical path, 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) is used as the radical-trapping agent and the formation of the desired product is suppressed, indicating that the reaction follows the radical pathway. The mechanistic pathway involves the generation of KSO_4 radical that reacts with the aldehyde to form a carbonyl radical. This carbonyl radical interacts with the indole molecule, and after subsequent steps, the final product is obtained by releasing the water molecule. In absence of Lewis acids and transition metals, this free-radical-based synthesis is well-suited with both unprotected and protected indole derivatives.



Scheme **1**. Synthesis of BIM using $K_2S_2O_8$

Chapter 3: Pd/C catalyzed C-2 selective direct functionalization of indoles with aryl iodides

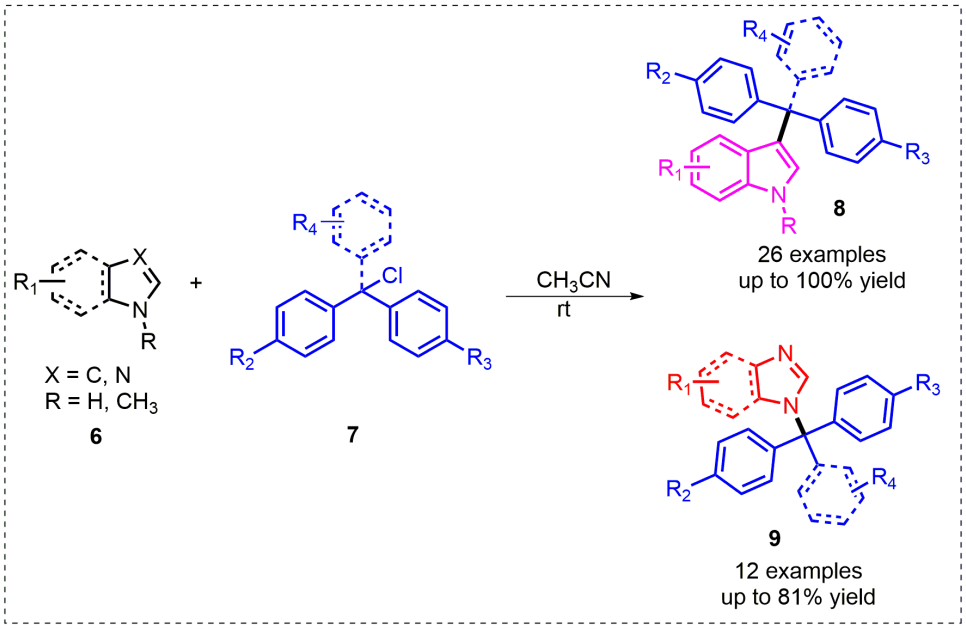
This chapter demonstrates the C-2 selective direct C(sp^2)-H bond functionalization of indoles (**1**) with aryl iodides (**4**) by using Pd supported on carbon (Pd/C) as a heterogeneous reusable catalyst (Scheme **2**). Arylation of indole at the C-2 position offers important synthetic intermediates of different bioactive compounds. In recent times, Pd/C has gained significant interest as a heterogeneous catalyst because of its attractive properties including easy availability, handling, recovery, and recyclability. Without using any ligand, additive, or directing group, our protocol exclusively furnishes C-2 arylated indoles (**5**). The current protocol shows better reactivity in the case of electron-rich substrates. The reaction initially involves the formation of Pd(II) species by oxidative addition of aryl iodide, which then reacts with indole to form an intermediate that undergoes 1,2 migration to afford the C-2 arylated product *via* reductive elimination. For a better understanding of the mechanistic pathway, we have carried out two control experiments, which indicates that initially electrophilic palladation takes place at the highly nucleophilic C-3 position of indole, and then undergoes 1,2 migration to form the desired product. The catalyst is reusable for up to four catalytic cycles with the retention of the catalytic efficiency.



Scheme **2**. C-2 selective direct functionalization of *N*-methylindoles

Chapter 4: Halogen bonding assisted C-3 benzylation of indoles and *N*-benzylation of imidazoles at room temperature

In this chapter, we explore a new protocol for C-3 selective benzylation of indoles (**6**) and and *N*-benzylation of imidazoles (**6**) using trityl chlorides (**7**) through halogen bonding under catalyst-free conditions at room temperature in acetonitrile (CH_3CN) (Scheme **3**). Benzylation at the nitrogen atom or at carbon atom of these *N*-heterocycles (indoles or imidazoles) offers biologically and pharmaceutically active compounds. Both protected and unprotected indole derivatives proceed the reaction with equal efficiency under the developed reaction conditions. The reaction failed in the case of C-3 protected *N*-methylindole indicating that the benzylation is only feasible at the C-3 position (**8**). In absence of an external base, trityl chlorides can easily benzylate imidazole derivatives at the nitrogen atom (**9**). Like trityl chloride, chlorodiphenylmethane is also an active benzylating agent for the current protocol. This transition metal-free methodology is applicable for a broad range of substrates with moderate to excellent yields (up to 100% yield) of desired products. With this catalyst-free methodology, the synthesis of a pharmaceutically active compound, **Clotrimazole** (antimycotic agent) is done and we can isolate the product up to 67% yield. The mechanistic pathway indicates the existence of halogen bonding which is further proved by UV-Vis and FT-IR analyses. The cleavage of the C-Cl bond is offered by CH_3CN because of its Lewis basic nature that acts as a halogen bond acceptor. This halogen bond acceptor binds with trityl chloride (halogen bond donor) to form a complex that reacts with indole (or imidazole) and finally results in the desired product. This simple and easy protocol is environmentally benign, affording the desired product under catalyst, base, and ligand-free conditions.

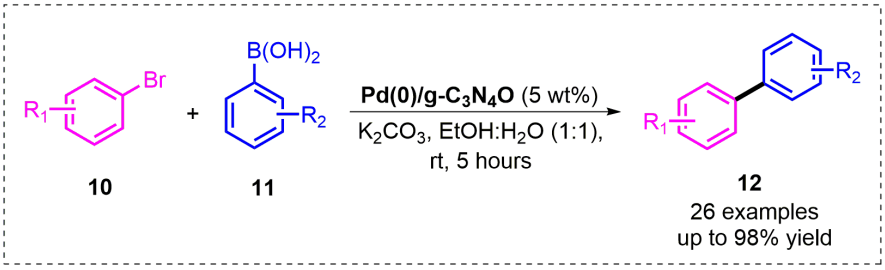


Scheme **3**. Selective C-3 and *N*-benzylation of *N*-heterocycles

Chapter 5: Exploring Pd(0)/g-C_3N_4O catalyzed Suzuki-Miyaura cross-coupling reaction with minimal base-stoichiometry

A study into the Pd nanoparticles (NPs) decorated on a graphitic carbon nitride oxide (g-C_3N_4O) sheet as an efficient heterogeneous catalyst for Suzuki-Miyaura cross-coupling reaction under limiting basic conditions is described in this chapter (Scheme **4**). The prepared biogenic catalyst, Pd(0)/g-C_3N_4O provides excellent yields (up to 98% yield) of the desired cross-coupled product (**12**) just under a sub-stoichiometric amount of exogenous base which is the highlight of this work. The Pd NPs are synthesized with the help of pomegranate (*Punica granatum*) peel extract which acts as a reducing and stabilizing agent for them. The graphitic sheet is derived from guanidine hydrochloride and it plays a pivotal role in the homogeneous dispersion of Pd NPs, thereby enhancing its catalytic activity. The g-C_3N_4O sheet is expected to perform two important functions. First, it directs the aryl bromides (**10**) towards the surface absorbed electron-rich Pd NPs and thus accelerates the oxidative addition step. The aryl bromide interacts with the π-π stacked layers of g-C_3N_4O and thus remains in close vicinity of the Pd NPs. Second is the activation of the arylboronic acid. The nucleophilicity of the organoboron (**11**) can be increased through its nitrogen or oxygen lone pairs to form the borate ion; thus acting as a pseudo-base and facilitating the overall reaction in minimum equivalents of an exogenous base. The synthesized catalyst is characterized by FT-IR, p-XRD, SEM-EDX,

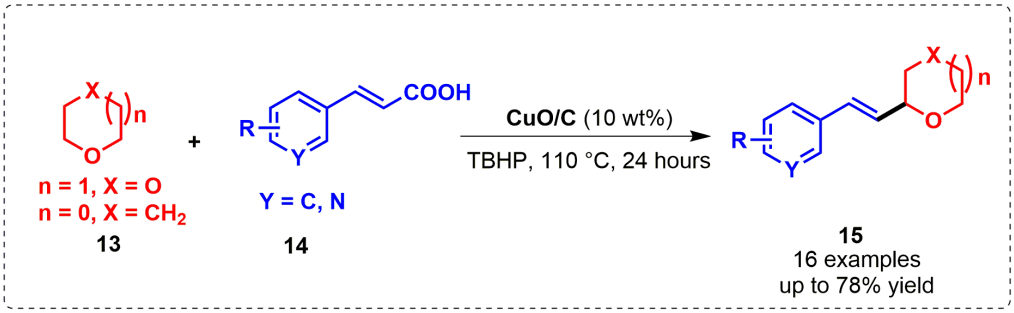
TEM, XPS, and BET analyses. Further, this bio-based catalyst is reused for up to five consecutive reaction cycles without significant loss of its catalytic activity.



Scheme **4**. Pd(0)/g-C_3N_4O catalyzed biaryl synthesis

Chapter 6: CuO/C catalyzed decarboxylative alkenylation of cyclic ethers

This chapter discusses about the synthesis of CuO NPs supported on carbon material and the utilization of the nanocomposite in the direct C(sp^3)-H bond functionalization of cyclic ethers (**13**) through decarboxylation by using electronically diverse cinnamic acid derivatives (**14**). Owing to its regiospecific nature, decarboxylative functionalization of the C−H bond is one of the most significant transformations in organic synthesis. The CuO/C nanocomposite is synthesized with the help of orange peel extract, which acts as a reducing and stabilizing agent, through the hydrothermal method without using any external mediator. In our methodology, only trans-configured (*E*) products (**15**) are obtained which is confirmed from the NMR spectra. The synthesized catalyst is characterized by different experimental techniques including, p-XRD, SEM-EDX, TEM, and XPS. The reaction fails in addition of TEMPO signifying that the mechanism follows a free radical pathway. This functionalization demonstrates well-tolerance towards different functional groups under ligand and base-free conditions.



Scheme **5**. CuO/C catalyzed decarboxylative functionalization of cyclic ethers

Chapter 7: Conclusion and future prospects

This chapter accomplishes the summary of all the above work along with the future viewpoints to extend the current work and explore new findings.