

Development of Catalytic Strategies for Selective Functionalization of Indoles and Related N-Heterocyclic Compounds

A thesis submitted in partial fulfilment of the requirement
for the award of degree of

Doctor of Philosophy

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November 2023

Chapter 6

Conclusion and Future Scopes

6.1 Conclusion

The prime focus of this thesis converges towards functionalization of indoles and related *N*-heterocyclic compounds through explorations in transition-metal based and metal-free catalytic processes.

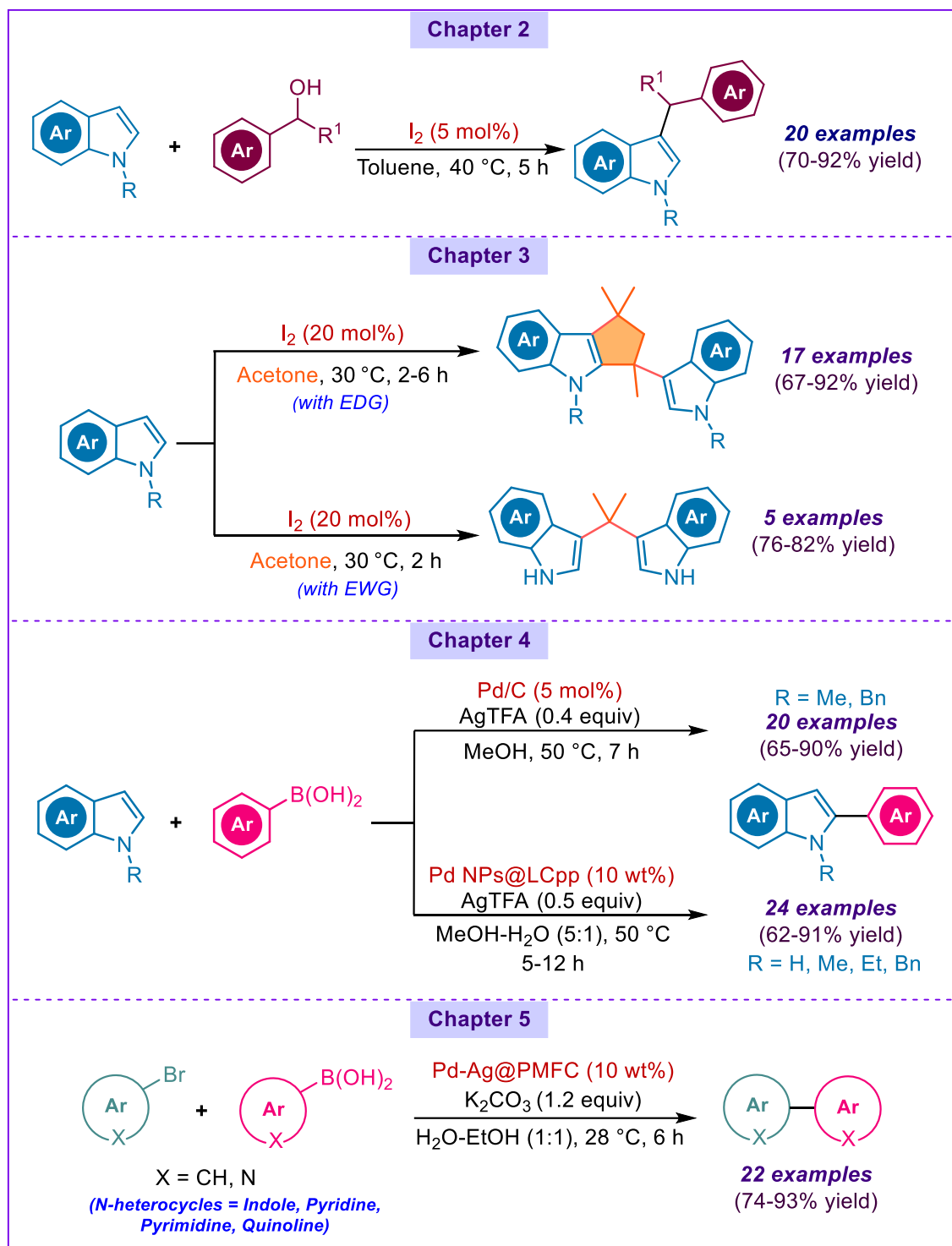


Figure 6.1 Schematic outline of experimental chapters

6.2 Significant Findings of the Experimental Works

The thesis is divided into six chapters: Introduction (**Chapter 1**), four experimental chapters (**Chapter 2-5**), conclusion and future scopes (**Chapter 6**). The significant outcomes of each chapter are highlighted below.

Chapter 2

- ❖ A molecular iodine catalyzed protocol for C3-benylation of indoles with benzyl alcohols.
- ❖ Environmentally benign method and proceeds under ligand-, metal-, and base-free conditions.
- ❖ Experimental observations accounts for halogen-bond activation pathway of iodine catalysis.

Chapter 3

- ❖ Substrate-controlled synthesis of cyclopenta[*b*]indoles under the catalysis of molecular iodine at room temperature.
- ❖ High-density electronic core of indole favours the formation of indolyl-cyclopenta[*b*]indoles, whereas electron deficiency of the core directs the reaction to bis(indolyl)propanes.
- ❖ Mechanistic investigations revealed bis(indolyl)alkanes to be the key intermediate for the cascade addition-intramolecular cyclization reaction.

Chapter 4

- ❖ Exploring two heterogeneous Pd-based catalytic systems for C2-arylation of indoles with arylboronic acids under ligand and directing group-free strategies.
- ❖ Section A employs commercially available 10% Pd/C as catalyst in presence of silver trifluoroacetate oxidant for the arylation of *N*-substituted indoles.
- ❖ Section B demonstrates sustainable preparation of Pd-supported on lignocellulose derived from waste pomegranate peels, for site-selective arylation of *N*-substituted and free *N*-H indoles.

- ❖ The methodologies displayed the potential of catalyst reusability with the scope for minimizing the amount of Ag oxidant throughout the re-cyclability course.

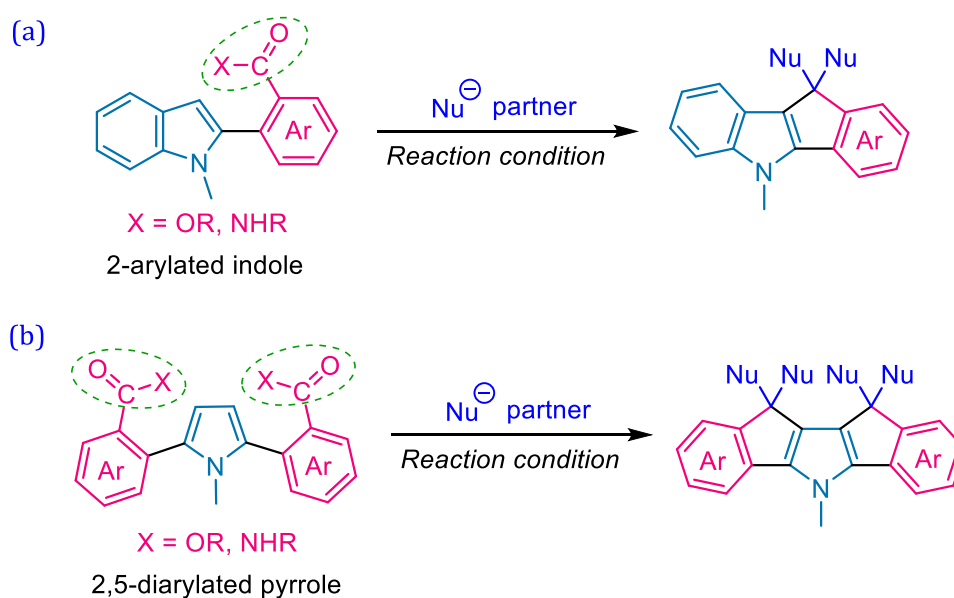
Chapter 5

- ❖ Describing a sustainable and biocompatible approach for the extraction of cellulose fibres from biomass waste using a simple ethanol-water filtration technique.
- ❖ The pomegranate peel derived cellulose micro-fibres presented as an admirable support matrix for bimetallic Pd-Ag nanoclusters.
- ❖ The heterogeneous-catalyst is explored for photocatalytic Suzuki–Miyaura coupling reaction of nitrogen-rich heterocycles *via* visible light mediated localized surface plasmon resonance (LSPR) at room temperature.

6.3 Future Scopes of the Works

The works described in the thesis have the potential to be extended in streamline organic synthesis. Accordingly, the future scope of the works is demonstrated below.

- The 2-arylated indole and 2,5-diarylated pyrrole derivatives can be modulated to corresponding fused-ring conjugated systems containing bridging carbon and nitrogen atoms, by careful selection of arylboronic acid coupling partner bearing a carboxamide or ester functionality at its 2-position (Scheme 6.1).



Scheme 6.1 Future scope of (a) 2-arylated indoles, and (b) 2,5-diarylated pyrroles

In presence of a suitable nucleophile partner, addition followed by an intramolecular cyclization can lead to generation of highly conjugated heterocyclic units.

- ii. The implicit challenges in accessing the less activated benzene ring regioselectivities (C4-C7 positions) in indole is evident from the limited number of methods that appears in the literature. Hence, more vibrant and divergent C–H activation methods to expand its scope to different classes of directing groups to target site-selective functionalization at the remote benzene ring positions (Figure 6.2).

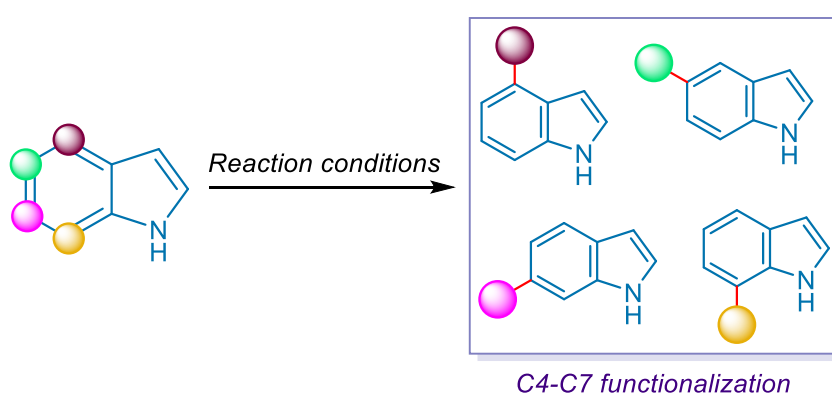


Figure 6.2 C–H functionalization at C4-C7 positions of indole

- iii. The integration of photocatalysis with transition metal chemistry has unlocked as a sustainable platform in modern molecular syntheses. Heterogeneous plasmonic photocatalysts harvest the energy of visible-light and transfer the energy for activation of reactants in a chemical reaction. The surface of metallic nanoparticles (Au, Ag, Cu) that supports collective electronic (plasmon) resonances, creates a local environment where chemical transformations can occur with unusual high efficiencies, and at milder temperatures than required for conventional catalysts. Hence heterogeneous photo-enabled plasmonic C–H activation processes can surface as a major innovation in this field for addressing previously inaccessible transformations in presence of a suitable source of light.

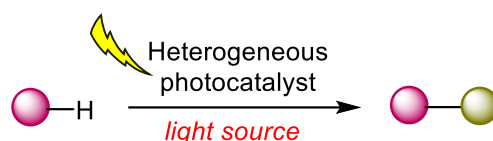


Figure 6.3 Heterogeneous photocatalytic C–H activation process