Multicomponent Synthesis of N-Containing Heterocyclic Compounds

THESIS SUBMITTED IN PARTIAL FULFILLMENT FOR THE AWARD OF DEGREE

DOCTOR OF PHILOSOPHY

By

HIMANSHU KUMAR SINGH

Department of Chemistry
Indian Institute of Technology
(Banaras Hindu University)
Varanasi-221005

Roll No: 17051017

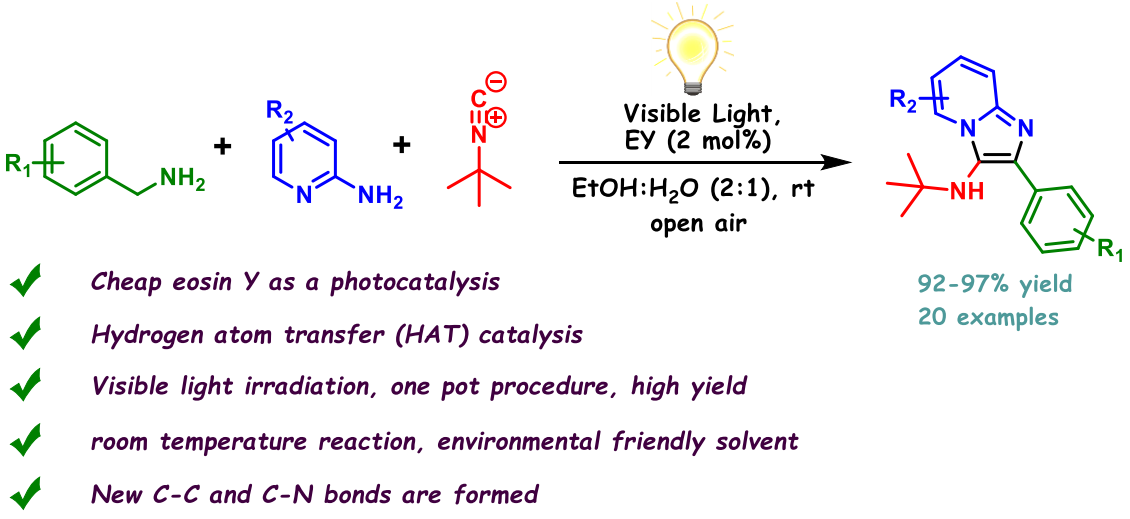
Year of Submission: 2023

Summary and Conclusions

The thesis entitled "**Multicomponent Synthesis of N-Containing Heterocyclic Compounds"** described the effective green synthesis of biologically active Nitrogen-containing heterocyclic compounds. The contents of the thesis have been divided into six chapters.

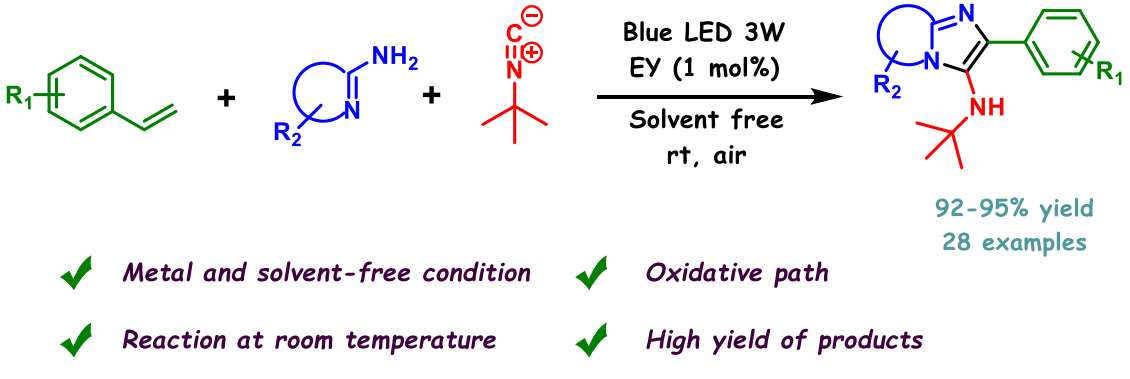
Chapter 1 provides a detailed explanation of multicomponent synthesis and its significance in organic synthesis, N-containing heterocycles and their importance, and different methods for synthesizing Nitrogen-Containing Compounds. The following four chapters describe the studies and conclusions (Chapters 2 through 5). Each chapter, which is utterly complete in itself, consists of an introduction, results and discussion, control experiment, mechanism, experimental section, and references.

Chapter 2 describes a simple, green, eco-friendly, highly efficient, inexpensive process for the synthesis of 3-aminoimidazo[1,2-a]pyridines from benzylamine, 2-aminopyridine, and *t*-butylisocyanide at room temperature using eosin Y as a photoredox catalyst under visible light. Due to the low cost, easy handling, and environmentally friendly nature of eosin Y has been used as an economically and ecologically superior photocatalyst alternative to transition metal complexes in organic photochemistry. This approach presents a promising alternative to the existing method, accordingly extending the scope of photocatalyzed reaction, which overcomes the problem associated with the environmentally notorious metal-catalyzed reaction. This approach was also validated on gram scale synthesis. (**Scheme 6.1**)



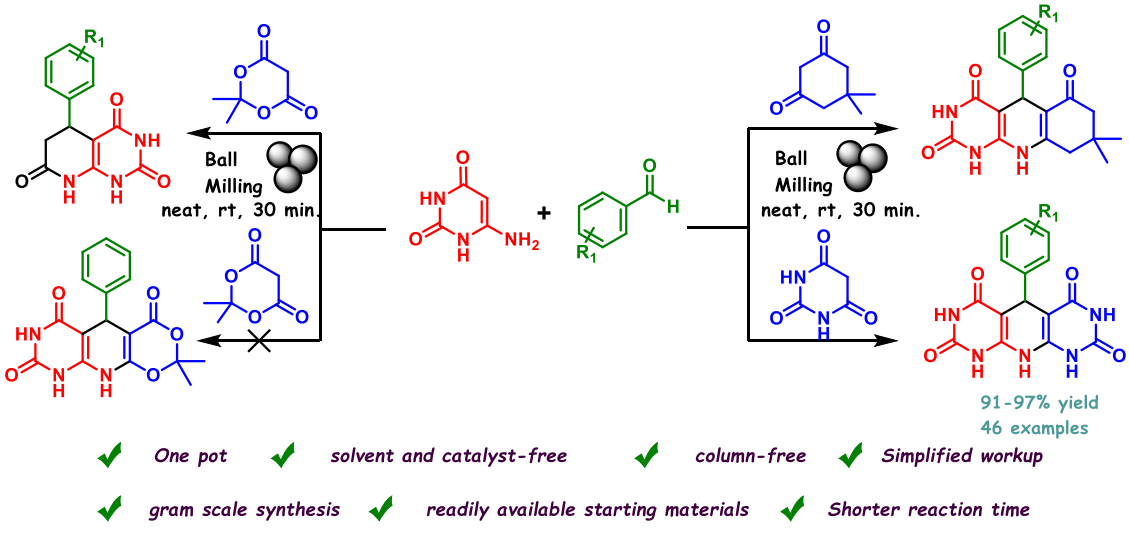
Scheme 6.1 Synthesis of 3-aminoimidazo[1,2-a]pyridines

Chapter 3 describes a mild, efficient, solvent-free, metal-free, and operationally simple visible light-promoted multicomponent reaction of styrene, 2-aminopyrimidine, and *t*-butylisocyanide has been developed for the synthesis of fused imidazoheterocycle using Eosin Y as a photocatalyst. This reaction is also valid for gram-scale synthesis of imidazoheterocycle. **(Scheme 6.2)**



Scheme 6.2 Synthesis of fused imidazoheterocycle

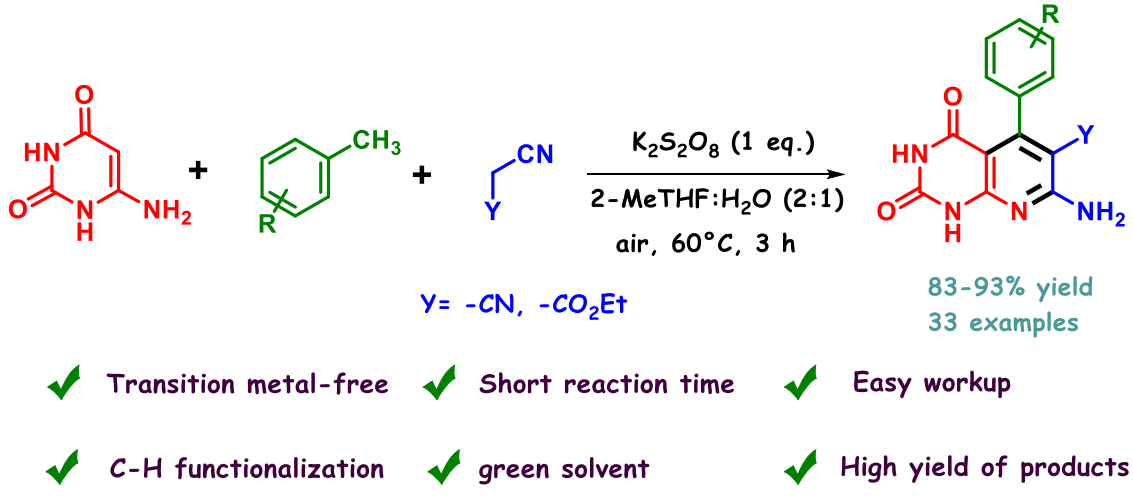
Chapter 4 describes a cost-effective and competent approach that has been established for the synthesis of N-heterocyclic pyrimido [4,5-b] quinolines and pyrido [2,3-d] pyrimidines via multicomponent reaction of 1,3 diketones (dimedone, barbituric acid and Meldrum's acid), 6-aminouracil and aromatic aldehyde, through mechanochemical synthesis using ball-mill. This transformation involves one pot, catalyst-free, and solvent-free pathway to develop desired products under mild reaction conditions. This approach was also validated on gram scale synthesis. **(Scheme 6.3)**



Scheme 6.3 Synthesis of N-heterocyclic pyrimido [4,5-b] quinolines and pyrido [2,3-d] pyrimidines

Chapter 5 describes a variety of Pyrido[2,3-d]pyrimidines derivatives that have been synthesized via Csp^3/Csp^2-H functionalization of readily available methyl arenes, 6-amino uracil, and malononitrile using $K_2S_2O_8$ under metal-free and environmentally benign conditions. By using methyl arenes as the C4 source of the Pyrido[2,3-d]pyrimidines skeleton, this synthetic strategy provides a series of Pyrido[2,3-

d]pyrimidines via an oxidative [3+2+1] cyclization process. This approach was also validated on gram scale synthesis. (Scheme 6.4)



Scheme 6.4 Synthesis of Pyrido[2,3-d]pyrimidines

All the demonstrated protocols in the thesis are superior to most existing protocols in terms of reaction condition and yield. Innocuous reagents, convenient procedure, and high yield make these methods more attractive in organic synthesis. Hence, the developed methodologies will find wide applications in organic synthesis.

Scope for Further Work

1. The power of visible-light-induced chemical reactions has long piqued the interest of chemist. Because of the chemical reactivity of electronically excited molecules not from the fundamemtal ground state, photochemistry has the potential to unlock reaction manifolds that are not accessible via traditional thermal pathways.

2. Further, explore the methylarenes as a surrogate for the construction of some privileged compounds.
3. Development of different methodologies like the mechanochemical approach, the metal-free, solvent-free reaction to synthesize N, S, and O containing biologically active compounds.
4. Further, explore the benzylamine as a surrogate for creating some privileged compounds.