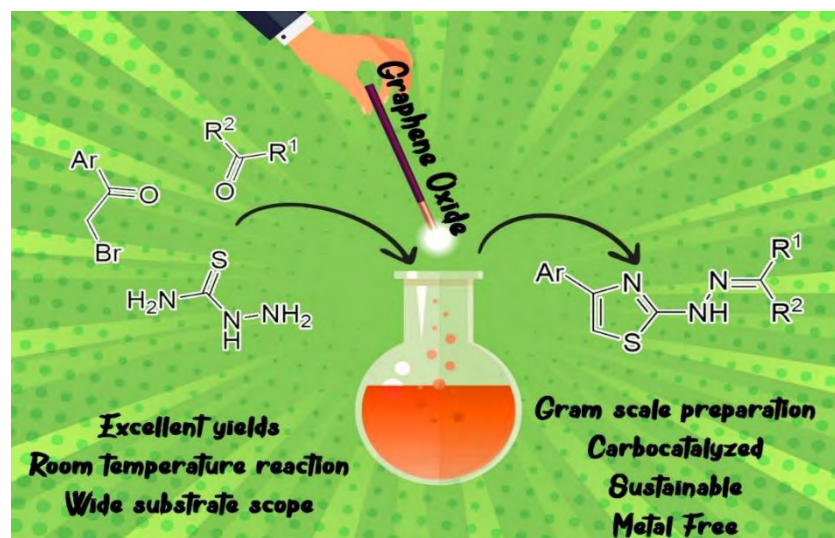


ABSTRACT

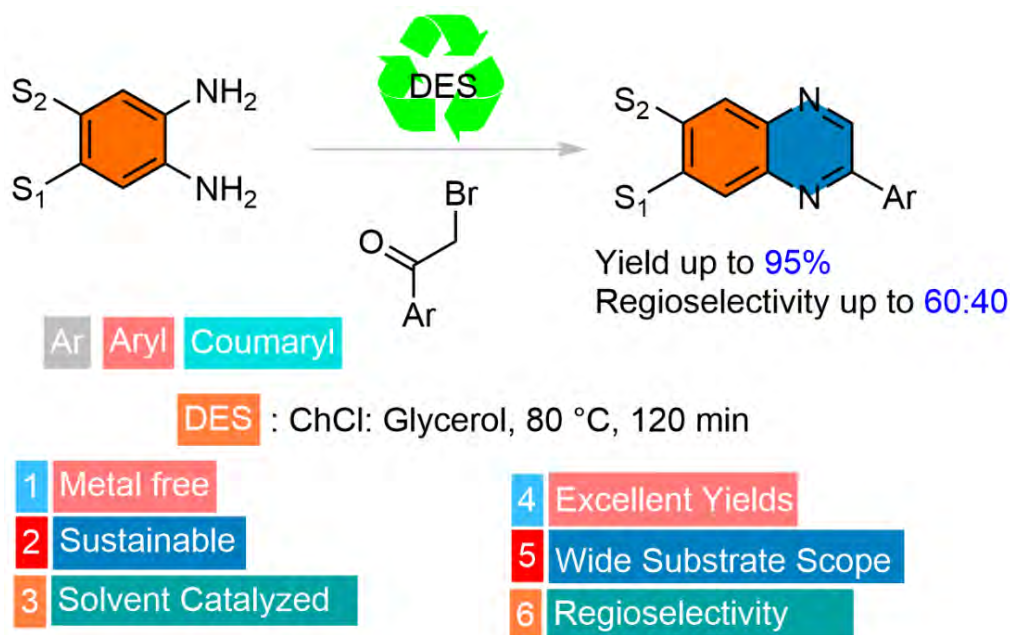
The journey toward the Ph.D. started in January 2020, it took almost five years to accomplish the research work included in the thesis entitled “**Design and Development of Synthetic Methodologies for Medicinally Privileged Heterocyclic Scaffolds**”. The entire thesis has been divided into five different chapters.

Chapter I primarily focuses on the concise review of various synthetic methodologies for medicinally important heterocyclic compounds by the reaction of various precursors. Heterocyclic compounds are the core moiety in most of the commercially available drugs. Apart from their medicinal use, heterocyclic compounds have also been used widely in material preparation, agrochemical synthesis, and the development of new fluorescent chemosensors.

In **Chapter II**, an efficient, one-pot three-component reaction in the synthesis of a wide range of 2,4-disubstituted hydrazinyl thiazole scaffolds in ethanol at room temperature has been developed by the reaction of carbonyl compounds, phenacyl bromides, and thiosemicarbazide, using graphene oxide (GO) as a catalyst. The present catalytic method has many significant advantages such as shorter reaction time, broad substrate scope, low catalyst loading, environmentally benign solvent media, easy handling, and operational simplicity at room temperature. The products are identified based on their various spectroscopic data. The GO catalyst has a high reusability rate and is simple to recover. A mechanistic study suggests that the reaction takes place *via* a thiosemicarbazone intermediate, which is isolated and confirmed in this study using spectroscopic techniques. Thereafter, a molecular docking study has been performed to evaluate the binding affinity of hydrazinyl thiazole derivative as a possible inhibitor on the protein active site of human α -amylase and glucosamine 6-phosphate synthase.

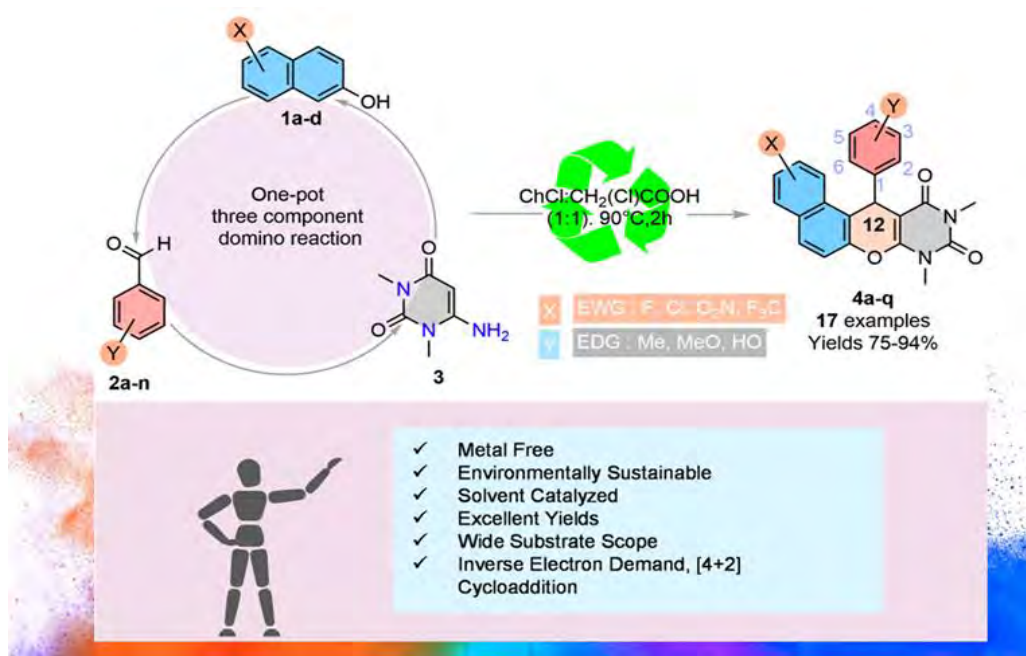


In **Chapter III**, A facile and eco-friendly sustainable synthesis of functionalized quinoxaline derivatives from 1,2-diaminobenzenes and 2-bromoacetophenones *via* a one-pot two-component reaction using choline chloride (ChCl): glycerol as a bio-renewable Deep Eutectic Solvent (DES) has been developed. In this protocol, nucleophilic 1,2-diaminobenzenes are mixed with phenacyl bromides or 3-(bromoacetyl) coumarin to produce quinoxaline derivatives in a high yield (up to 96%), with a clean reaction profile without the use of a solvent or catalyst at ambient temperature (80 °C). The presence of DES is proven to be essential for assuring efficient transformation, as the product yield was extremely low with a slow reaction profile in the absence of this media. The DES media could be recycled and reused up to five times without losing its efficiency or affecting the chemical yield of the reaction. In the showcase study, the reaction was also scaled up to the gram scale (10 mmol scale), revealing the synthetic potential of the current approach. A density functional theory (DFT) calculation has been also performed to probe the mechanism and reversal of the regioselectivity in the products formation.



In **Chapter IV**, A novel, one-pot, three-component coupling (3-CCR) reaction of aromatic aldehydes, β -naphthol, and 6-amino-1,3-dimethyl uracil in Deep Eutectic Solvent (DES) has been developed as a highly efficient and selective method for the expedient synthesis of densely functionalized 8,10-dimethyl-12-phenyl-8,12-dihydro-9H-benzo [5,6] chromeno[2,3-d] pyrimidine-9,11(10H)-dione framework in synthetically pleasing yield. The devised protocol

adeptly harnesses the versatility of DES, resulting in a straightforward, cost-effective, resilient, and environmentally sustainable synthetic approach. The resulting cascade adduct exhibits noteworthy antiproliferative activity against a variety of cancer cell lines, thereby showing promise as a potential anticancer drug candidate for breast and hepatocellular carcinoma with moderate to good IC₅₀ values. The most potent compounds in the synthesis library, **4m** and **4l**, exhibit highly potent cytotoxicity against HepG2 and MCF7 cancer cell lines, with notable IC₅₀ values of 46.39 and 28.21 μ M, respectively. Further the present findings are further substantiated by computational and molecular docking studies of which, density functional theory (DFT) calculations underscore the pivotal role of the naphthyl ring in orchestrating the success of this intricate domino process in delivering the anticipated scaffolds in reasonable yields.



In **Chapter V**, an environmentally benign one-pot three-component synthetic strategy has been developed for a diverse range of pyrimidobenzothiazoles by the reaction of 2-amino benzothiazole, β -keto ester, and aldehydes in $\text{ChCl}:\text{Malonic acid}$ (1:1) based deep eutectic solvent (DES) medium. This newly developed methodology has several advantages i.e. excellent yield of product, clean reaction profile, quick reaction time, easy handling, and wide substrate scope. All of the synthesized compounds have been extensively characterized with various spectroscopic techniques. To check the synthetic potential scale up study has also been performed, which provided a pleasing yield of pyrimidobenzothiazole even on the gram scale.

Above all DES medium can be easily recovered and reused for up to four consecutive cycles without any substantial change in product yield.

