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Title:	Nucleophilic Carbene Catalysis in Chemoselective & Aerobic Oxidation Reactions
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**Abstract:** This thesis work is divided in to two parts, Part A and Part B. Part A deals with chemoselective transformations catalyzed by nucleophilic carbenes and Part B deals on the organic transformations under oxidative N-heterocyclic carbene (NHC) catalysis. PART A: Chemoselective transformations catalyzed by nucleophilic carbenes Part A is divided in to three chapters. Chapter 1: General introduction on the N-heterocyclic carbene (NHC) catalysis: This chapter covers a concise review about the history, the modes of activation of N-heterocyclic carbenes toward carbonyl groups and applications of N-heterocyclic carbenes in organocatalysis. Scheme 1 portrays the different modes of activation of NHC toward various carbonyl compounds. Chapter 2: Chemoselective synthesis of trifluoromethylated acyloins using NHC as an organocatalyst: Although NHC catalyzed intermolecular homodimerization of aldehydes is well documented in the literature, intermolecular crossed acyloin condensation still remains as a challenge because of the mismatch between the reactivity of aldehyde and the coupling partner. Choosing a right coupling partner is crucial in the crossed acyloin condensation, otherwise the reaction would lead to four different acyloins including two homodimerized products. A very few successful reports are available in the literature for the intermolecular crossed acyloin condensation in which the coupling partner was aldehyde or ketone. But so far, no reports are available using hemiacetals as an “aldehyde equivalent” (as a coupling partner) in intermolecular crossed acyloin condensation. This chapter deals with N-heterocyclic carbene (NHC) catalyzed a highly chemoselective intermolecular crossed acyloin reaction of various aldehydes with trifluoroacetaldehyde ethyl hemiacetal (as a coupling partner) leading to trifluoromethylated acyloins. Trifluoroacetaldehyde ethyl hemiacetal is relatively stable and commercially available (as 90% aq. solution). Moreover, this particular hemiacetal introduces trifluoromethyl group in the acyloin product, which could be easily transformed to pharmaceutically important trifluoromethyl containing heterocycles or drugs. The substrate scope for this reaction was evaluated using a wide range of aromatic aldehydes, and almost in all cases, the required trifluoromethyl containing acyloins were obtained in good to excellent yields with >95:5 high chemoselectivity (Scheme 2). To show the synthetic utility of this methodology, one of the crossed acyloin product was converted into trifluoromethyl containing quinoxoline (Scheme 3). An enantioselective version of the intermolecular crossed acyloin reaction between pchlorobenzaldehyde and trifluoroacetaldehyde ethyl hemiacetal was also performed in the presence of a few chiral NHCs as a catalyst under various reaction conditions. In one of the reaction conditions, the crossed acyloin product was obtained with the maximum of 30% ee. Chapter 3: Bis(amino)cyclopropenylidene (BAC) catalyzed chemoselective synthesis of  $\alpha,\alpha'$ -diarylated ketones: This chapter describes a brief introduction about the synthesis, stability, reactivity and applications of bis(amino)cyclopropenylidenes (BACs) in organometallic chemistry<sup>4</sup> as well as in organocatalysis. It has been realized that the NHCs based on a heterocyclic core such as thiazole, triazole, imidazole etc. are dominating in organocatalysis due to their unmatched nucleophilicity and high stability. On the other hand, bis(amino)cyclopropenylidene, which is a smallest aromatic compound with an inherent carbene center, was found to be a promising nonheterocyclic based candidate in terms of reactivity towards metals and carbonyl compounds. Though bis(amino)cyclopropenylidenes have been widely explored as a ligand in organometallic chemistry,<sup>4</sup> only a few reports are available in the literature on the application of bis(amino)cyclopropenylidenes as organocatalyst. This chapter also describes a mild and efficient method for the synthesis of  $\alpha,\alpha'$ -diarylated ketones via intermolecular 1,6-conjugate addition of aromatic aldehydes to p-quinone methides (p-QMs) using bis(amino)cyclopropenylidene as an organocatalyst. The versatility of this protocol has been portrayed using a wide range of aromatic and heteroaromatic aldehydes as well as p-QMs, and in all the cases, the corresponding  $\alpha,\alpha'$ -diarylated ketones were obtained in moderate to good yields under the optimized reaction conditions (Scheme 4). A plausible mechanism has also been proposed for this transformation. PART B: Organic transformations under oxidative N-heterocyclic carbene catalysis Part B is divided in to three chapters. Chapter 1: General introduction on the oxidative N-heterocyclic carbene (NHC) catalysis: Chapter 1 covers a general introduction about the oxidative N-heterocyclic carbene catalysis, a sub-area of N-heterocyclic carbene (NHC), which is emerging as one of the dominant methods for the construction of carbon–heteroatom (C–O, C–N) bonds. A few NHC catalyzed oxidative transformations is shown in scheme 5. Chapter 2: Aerobic oxidation reactions under oxidative NHC catalysis Chapter 2 is sub-divided in to two parts. (a) Tetraphenylphosphonium bromide as a phenyl source for the synthesis of phenyl esters under oxidative NHC catalysis: This part deals with the synthesis of aromatic esters from aromatic

aldehydes using Ph4PBr as a phenyl source through oxidative NHC catalysis. Although Ph4PBr has been utilized as a phenyl source for Pd-catalyzed coupling reactions, it has not been explored in esterification reactions. The optimization was carried out between p-chlorobenzaldehyde and Ph4PBr using different NHCs under different reaction conditions, and the NHC derived from SIPr.HCl (A) was found to be the best catalyst for this transformation (Scheme 6). The substrate scope and the mechanism for this reaction are discussed in detail. b) Synthesis of trimethylsilylmethyl esters under oxidative NHC catalysis: The synthesis of trimethylsilyl methyl esters starting from aromatic aldehydes and chloromethyl trimethylsilane under aerobic oxidative NHC catalysis has been described in this part. Out of many NHCs screened, the one derived from SIMes.HCl (A) was found to be the best. A wide range of aromatic aldehydes have been converted to their corresponding trimethylsilyl methyl esters in moderate yields under the reaction conditions (Scheme 7). Chapter 3: Combining oxidative NHC catalysis with click chemistry to access 1,2,3-triazole derivatives: This chapter deals with the one-pot synthesis of 1,2,3-triazole derivatives by merging oxidative NHC catalysis with click chemistry. Before exploring the one-pot process for the synthesis of 1,2,3-triazoles, it was necessary to optimize the first step, i.e. propargyl ester formation. Thus, the esterification reaction was optimized under aerobic conditions and the substrate scope was evaluated using a wide range of aldehydes and propargyl bromides (Scheme 8). This protocol was then elaborated for the one pot synthesis of 1,2,3-triazole derivatives by combining with copper catalyzed click chemistry. This one-pot method was found to be versatile as a wide range of 1,2,3-triazole derivatives have been generated in good yields (Scheme 9).

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