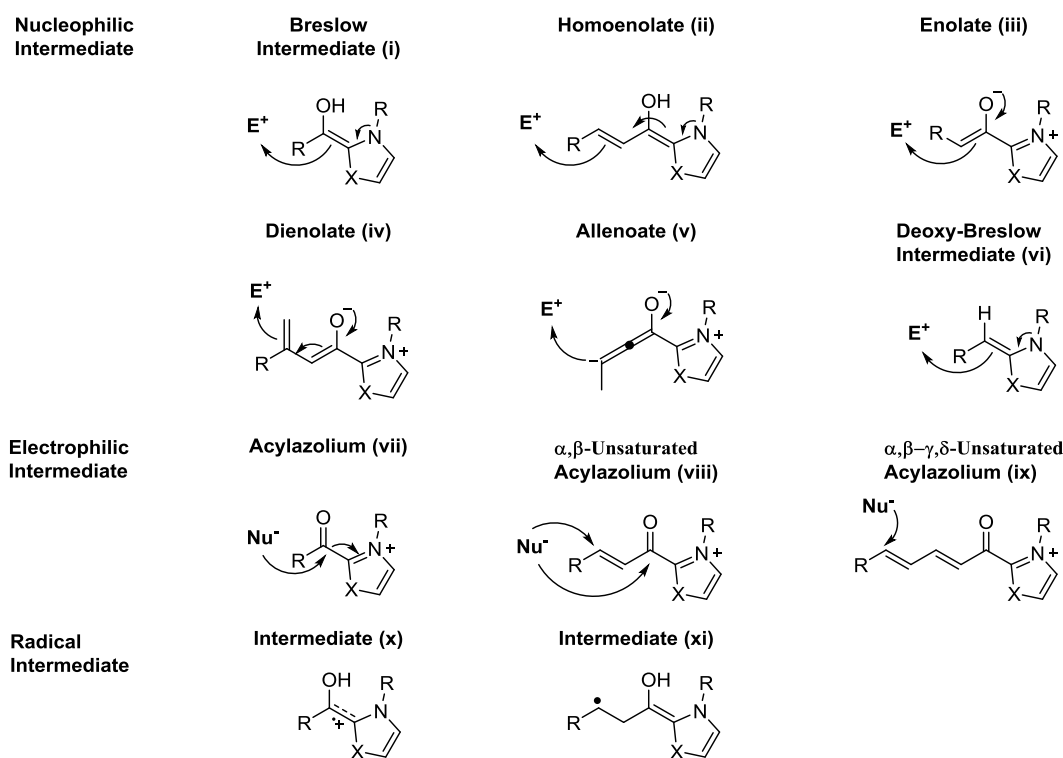


The thesis entitled “**Development of new synthetic methods via *N*-heterocyclic carbene catalysis**” is divided into three chapters.

Chapter I: An Introduction to *N*-Heterocyclic Carbene (NHC) Catalysis

This chapter provides a brief overview about *N*-heterocyclic carbene (NHC)-catalysis and its various reactivity modes (Scheme 1.1). NHC-based organocatalysts have emerged as one of the important synthetic tools for the construction of various carbon-carbon and carbon-heteroatom bonds through umpolung, non-umpolung and radical strategy. NHCs in organocatalysis are typically involves the use of numerous NHC-bound nucleophilic intermediates such as acyl anion, homoenolate, enolate, dienolate, allenolate and deoxy Breslow intermediate (Scheme 1.1). The benzoin condensation and Stetter reaction are the two most prominent reactions, which utilize the acyl anion intermediate (i). Moreover, a variety of acyclic as well as annulated products, mostly in asymmetric form, have been accessed from simple starting materials with the employment of NHC-bound reactive nucleophilic intermediates (ii-vi). Apart from the umpolung strategies, NHCs are also used as a catalyst for the generation of diverse electrophilic intermediate such as acyl azolium, α,β -unsaturated acyl azolium and $\alpha,\beta,\gamma,\delta$ -unsaturated acyl azolium (vii-ix) form the corresponding unsaturated carbonyl compounds in the presence of external oxidant. In most of the cases, these important reactive intermediates acts as a bis-electrophile and thus allowing the nucleophilic addition of several bis-nucleophile in a 1,4-fashion followed

by 1,2-pathway for the unconventional construction of various carbocycles and heterocycles which are not suitable in presence of other covalent organocatalysis. In spite of two electron pathway, NHCs are also used in single electron transfer pathway for various important transformation through acyl radical and homoenolate radical intermediate (x and xi). Importantly, these reactive radical intermediates enabled the introduction of sterically bulky substituents, which are not compatible in the well-known two-electron reaction pathway under NHC catalysis.

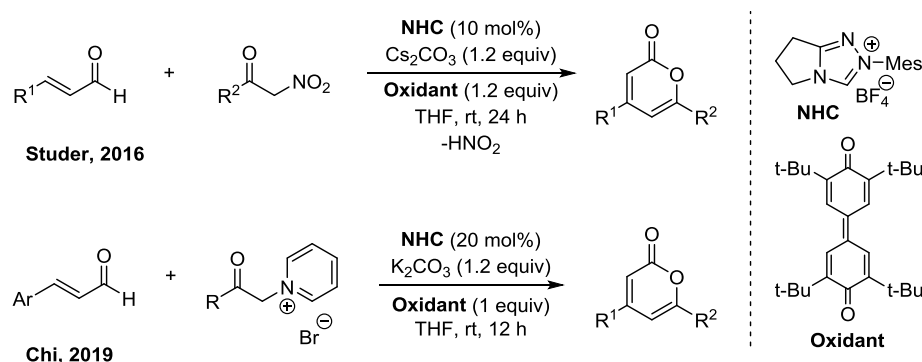


Scheme 1.1 Various important reactivity modes of NHC

Chapter II: A Facile Access to 3,6-Disubstituted α -Pyrone via Carbene Catalyzed Formal [4+2] Annulation of α -Chloroaldehydes and γ -Keto Sulfones

This chapter is divided into two parts *i.e.* Part-A and Part-B.

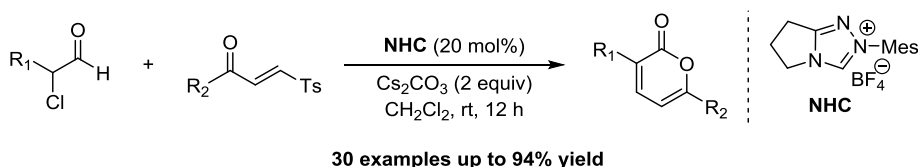
Part A of chapter II entitled “*Introduction to α -pyrones and preparation of starting reagents*” provides a brief sketch about the importance of α -pyrones. The construction of α -pyrone motifs is of great interest due to their utility in the preparation of various key intermediates in synthetic organic chemistry as well as medicinal chemistry. This chapter describes the literature reported methods for the preparation of α -pyrones under metal-based or metal-free catalytic system. Notably, the previous NHC-catalyzed protocols provided 4,6-disubstituted α -pyrones under oxidative conditions (Scheme 1.2). To the best of our knowledge, an NHC-catalytic oxidant-free synthetic method for the synthesis of 3,6-disubstituted α -pyrones has never been reported thus far. Therefore, we envisioned the challenging 3,6-disubstituted α -pyrones under oxidant-free NHC-catalysis using simple starting materials such as α -chloroaldehydes and γ -keto sulfones.



Scheme 1.2 Synthesis of 4,6-disubstituted α -pyrones using oxidative NHC-catalysis

Part B of chapter II entitled “*Introduction to NHC-bound enolate intermediate and its application to access 3,6-disubstituted α -pyrones*” provides an overview about reactions involving NHC-bound enolate intermediate and its implementation for the synthesis of desired 3,6-disubstituted α -pyrones. The importance and generation of

NHC-bound enolate intermediate from various sources is described in this part. The employment of NHC-bound enolate intermediate for the synthesis of 3,6-disubstituted α -pyrones under oxidant free condition by the reaction of α -chloroaldehydes and γ -keto sulfones has been demonstrated in part B of this chapter (Scheme 1.3). Notably, a broad range of α -chloroaldehydes and γ -ketosulfones were tolerated under the optimized reaction conditions. The use of γ -keto sulfones as a Michael acceptor was key for this unique transformation, enabled the formation of desired α -pyrones in good to excellent yields under transition-metal-free reaction conditions. The present protocol proceeds through Michael addition followed by lactonization and elimination cascade sequence to furnish a variety of 3,6-disubstituted α -pyrones. In addition, this methodology is also demonstrated for the gram-scale synthesis of 3,6-disubstituted α -pyrone. Furthermore, the synthetic utility of the product to afford a variety of value-added molecules in good yields is also explored in this part.

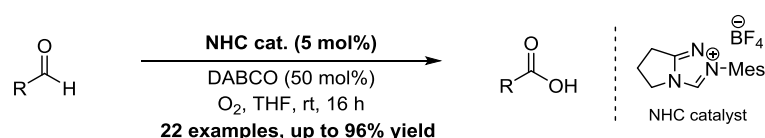


Scheme 1.3 NHC-catalyzed oxidant-free synthesis of 3,6-disubstituted α -pyrones

Chapter III: A Highly Efficient NHC-Catalyzed Aerobic Oxidation of Aldehydes to Carboxylic Acids

Carboxylic acids are one of the most privileged structural motifs that is present in various organic compounds used in industry for the production of pharmaceuticals, food additives, agrochemicals, polymer and solvents. This chapter outlined the literature known synthetic methods for the synthesis of carboxylic acids and its

derivatives through metal-based oxidants utilizing stoichiometric amounts, several metal-based or metal-free catalytic methods as well as generation and importance of NHC-bound reactive intermediates under oxidative catalysis. Notably, all the previous reports based on NHC-catalyzed oxidation of aldehydes to acids are suffered from one or more limitations such as limited substrate scope like primarily suitable for activated electron-deficient aryl or hetero-aryl aldehydes, require reaction time of several days and higher temperature. Therefore, an efficient NHC-catalyzed oxidation of aldehydes to carboxylic acids in the presence of oxygen as sole oxidant with a shorter reaction time at room temperature has been developed and described in this chapter (Scheme 1.4).



Scheme 1.4 NHC-catalyzed aerobic oxidation of aldehydes to carboxylic acids

Pleasingly, the compatibility of *ortho*-substituted or electron rich aryl aldehydes and indole-3-carboxaldehydes under environmental benign aerobic conditions intensify the novelty of the present protocol. Moreover, this methodology is also extended for gram-scale synthesis under the optimized reaction conditions.

Conclusion

In this section, the brief description with important characteristic and application of newly developed reactions are described. In addition, the advancement of these protocols and product classes in synthetic organic chemistry are also explained.