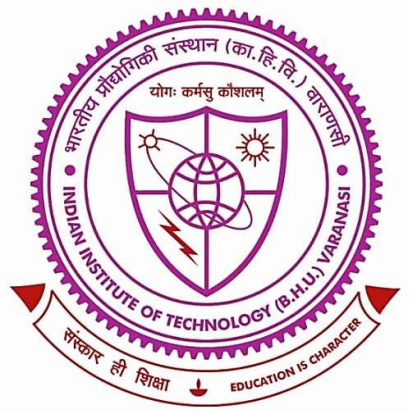
# Synthesis and Applications of *N*-Activated Amides in Different Organic Transformations




**Thesis submitted in partial fulfilment for the**

**Award of Degree**

**Doctor of Philosophy**

**by**

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# CHAPTER-6

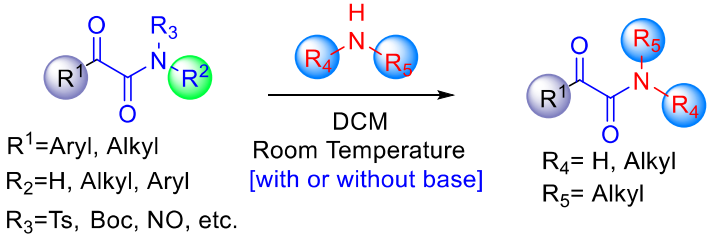
# Summary and Conclusions

## 6.1 Summary and Conclusions

The thesis entitled **"Synthesis and Applications of *N*-activated amides in different Organic Transformations"** described the preparation of *N*-activated carboxamides such as *N*-Boc, *N*-Ts, *N*-NO and *N*-Cbz and their applications in C-N, C-O and C-C bond formation reactions. The contents of the thesis have been divided into six chapters including summary and conclusion.

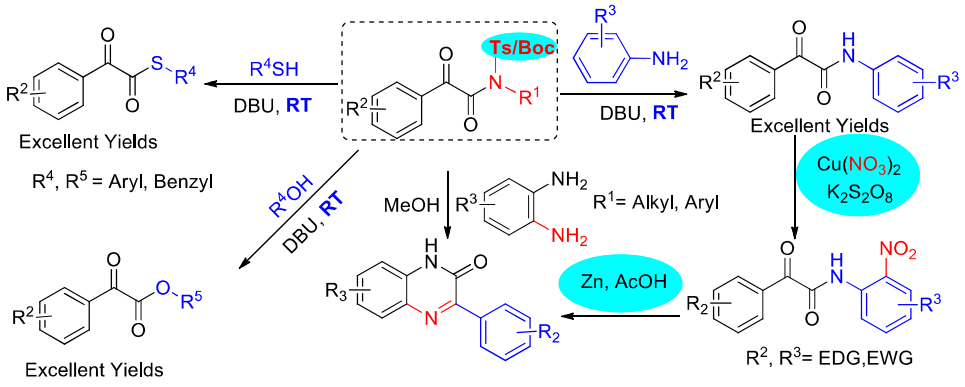
**Chapter 1** gave a general introduction of amides and their biological and synthetic application in organic chemistry. In addition, brief descriptions about the planner and twisted amides, activation of planner amides, etc. haven provided.

**In chapter 2,** transamidation reaction in *α*–ketoamides was demonstrated with a wide range of *N*-tosyl and *N*-Boc α–ketoamides at room temperature. Transamidation of *N*-tosyl *α*–ketoamides with alkyl amines carried out in the absence of catalyst, base or additives, while $Cs_2CO_3$was used in the case of *N*-Boc *α*–ketoamides (**Scheme 6.1**). A variety of alkyl, benzyl and aliphatic secondary amines underwent transamidation reactions under optimized condition with good to excellent yield. Broad substrate scope and excellent functional group tolerance are the merits of the developed methodology.




**Scheme 6.1** Transamidation of *α*-ketoamides with alkyl amines.

**The Chapter 3** described an efficient and promising strategy for the synthesis of *N*-aryl *α*-ketoamides *via* transamidation of *N*-Ts and *N*-Boc *α*–ketoamides with aromatic amines in the presence of DBU (**Scheme 6.2**).

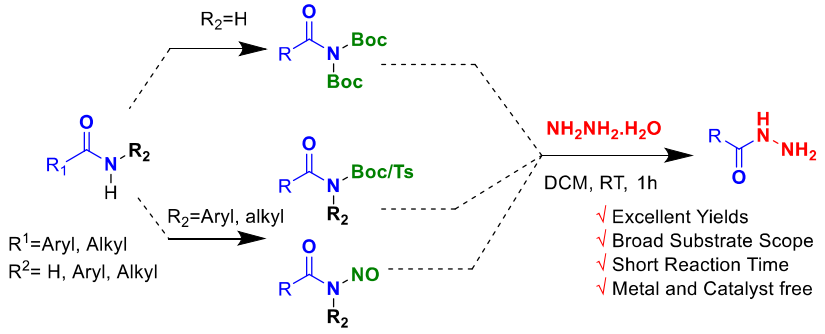



**Scheme 6.2** Summary of transformations in chapter 3.

Moreover, esterification of *α*–ketoamides with thiols and alcohols was also successfully achieved in excellent yields in the presence of DBU. A variety of aromatic amines substituted with electron donating and electron withdrawing groups, aromatic and aliphatic alcohols and thiols underwent transamidation/esterification reactions under optimized condition with good to excellent yield. Transamidation of *α*–ketoamides with *ortho*-phenylenediamine in methanol gave biologically relevant quinoxalinone molecules in excellent yields. Alternatively, *N*-aryl *α*–ketoamides were used as the substrates for the regioselective preparation of quinoxalinones in good yields via *ortho*-nitration with $Cu(NO_3)_2/K_2S_2O_8$ followed by reduction with Zn/AcOH.

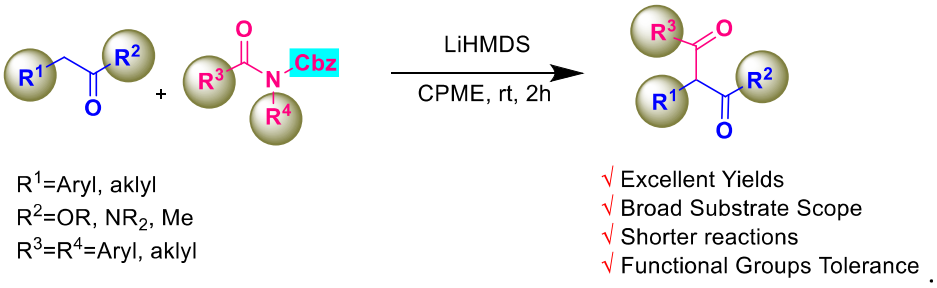
**In chapter 4,** synthesis of acyl hydrazides from amides have been achieved through *N*-activation reactions. A wide spectrum of functionalized primary and secondary amides was converted into *N*-Boc, *N*-nitroso and *N*-tosyl amides and subjected to

transamidation with hydrazine hydrate at room temperature to obtain the desired acyl hydrazides in 80-95% yields. Broad substrate scope, shorter reaction time and mild reaction conditions are the merits of the developed methodology (**Scheme 6.3**).




**Scheme 6.3** Transamidation of *N*-activated benzamides with hydrazine hydrate.

**The Chapter 5** disclosed a base-promoted C-C coupling reactions of wide range of functionalized *N*-Cbz amides with enolizable esters, ketones and amides to afford 1,3-dicarbonyl compounds under mild conditions (**Scheme 6.4**). The reactions proceeded at room temperature in the presence of LiHMDS in cyclopentyl methyl ether (CPME). The desired *β*-ketoesters, *β*-keto amides and 1,3-diketones were obtained in good to excellent yields in a short reaction time. Broad substrate scope, functional group tolerance and metal-free conditions are the merits of the developed methodology




**Scheme 6.4** Preparation of 1,3-dicarbonyl compoundsusing *N*-Cbz amides.

All the demonstrated protocols in the thesis are advancement of existing protocols in terms of reaction conditions and yield. Mild reaction conditions and 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.