

ABSTRACT

The toxicity and volatile nature of many organic solvents, particularly chlorinated hydrocarbons that are widely used in huge amounts for organic reactions have posed a serious threat to the environment. Thus, design of solventless multicomponent reaction has received tremendous attention in recent times in the area of green synthesis. It was with the objective of finding an easier, cheaper and efficient method for synthesis of compounds with potential industrial and pharmacological demand that the efforts culminated into this dissertation. Out of a range of choices from microwaves to ultrasonication, we narrowed down to the use of thermal methods involving thermo-chemical activation for developing our solvent-free protocol because of the simplicity of the technique and its possibility for up-scaling.

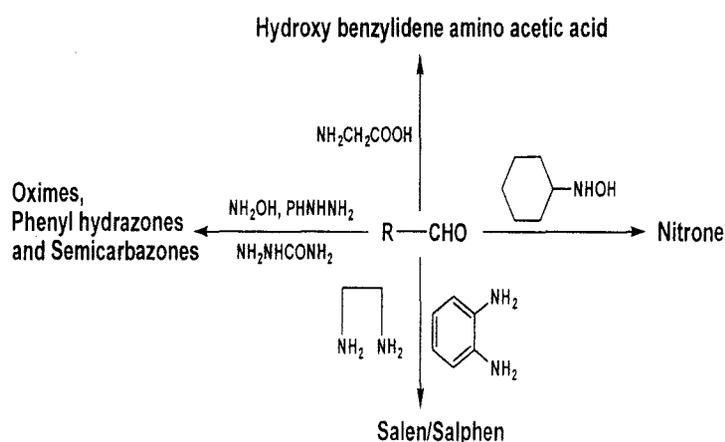
The dissertation entitled “Designing of Green Chemical Reaction Conditions using Thermal Analysis” is aimed at developing a benign synthetic strategy for the syntheses of various biologically and synthetically important compounds. The present work concentrates on multicomponent solventless synthesis via thermochemical activation. The synthetic procedures are accompanied by *a priori* thermal analysis of reaction mixtures to optimize reaction conditions for carrying out reaction under solvent-free conditions. The novelty of the methodology stands out in respect of its high yields, very short reaction time and the attempt to avoid as much as possible the use of solvents and extensive purification procedures.

The work has resulted in the synthesis of a large number of metal complexes via a solventless multicomponent approach. In the process of generating a rationale for reactions in condensed phase, the work culminated with a diversity oriented synthesis of a large number of Imidazole and its derivatives. The deliberation has been organized in three chapters.

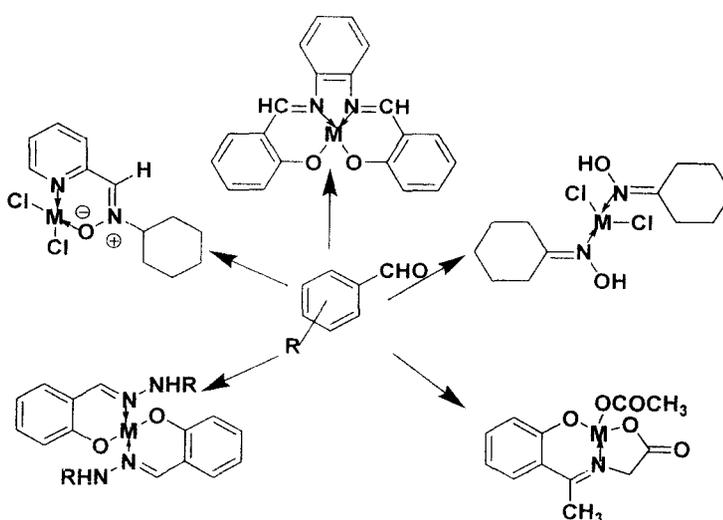
Chapter I includes a brief review on the concept of Green Chemistry and its principles, two benign methods in organic synthesis viz., Solventless reactions and Multicomponent synthesis

and finally a short introduction to Thermal analysis, since each of these concepts have been utilized in designing the methodology.

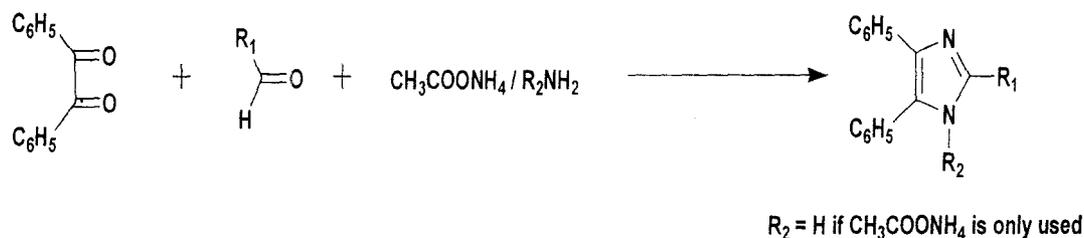
Chapter II is the main text of the thesis, including the results and discussions of the work. In the first section (2.2) of this work a methodology starting from optimization of reaction conditions based on a simple thermogravimetric analysis or a DSC analysis is shown in its utility to synthesize various Schiff bases and Schiff base type compounds.



The rationale was extended to the efficient synthesis of the transition metal complexes of these Schiff bases involving a multicomponent strategy with metal salts. Applying the principles of Green Chemistry has led us into extending the multicomponent synthesis for metal complexation, and establishing protocol for metal-coordinated organic frameworks.



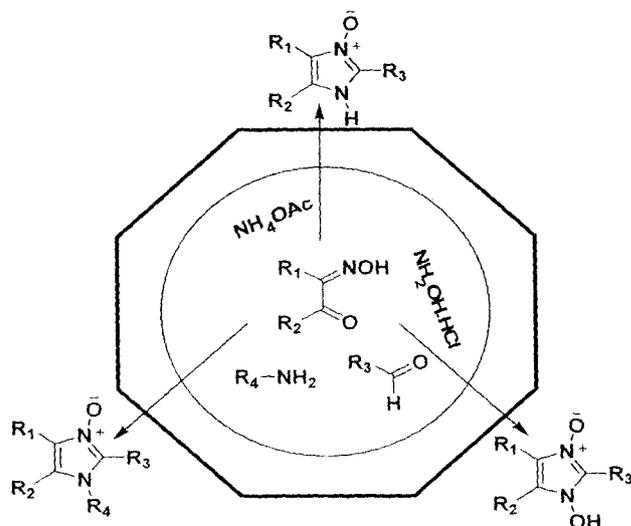
In the second section (2.3) of this work, the application of our protocol was extended to another condensation reaction leading to a versatile heterocycle, the Imidazole and its derivatives. Also the possibility of augmenting the optimization process with mechanistic insights in reactions under condensed phase was studied.



Towards this end, the technology of HPLC was found to be very useful as a method for efficient calculation of rate constants and indicating the presence of the reaction intermediates from the peak areas of the HPLC trace. Interestingly, HPLC has been used for kinetic studies of solid –state reactions only seldom. The kinetic studies from the present work revealed that the non-catalytic method was as effective as any other reported method for its preparation if carried out at a slightly higher temperature (optimized by the HPLC studies). At the optimized temperature the products could be formed within a very short time of 2-4 minutes with excellent yields of 99%.

The observation led us to propose that there could be a self catalytic effect of the carbonyl groups which led to the activation in the condensed phase. This was substantiated by quantum mechanical PM3 calculations which were found to agree with the experimental and spectroscopic results.

To further support our rationale of self-activation of carbonyls in the condensed phase, the work was extended further to the synthesis of the Imidazole N-oxides and the Hydroxy Imidazole N-oxides (Subsection 3.3.2.) The synthesis of N-substituted Imidazole N-oxide warrants the use of an amine compound instead of ammonium acetate while hydroxylamine hydrochloride is used during the preparation of the 1-hydroxyImidazole-3-oxide. All syntheses were carried out under solvent-free conditions with *a priori* TGA and DSC as well as STA studies.



Both the derivatives are conveniently formed in quantitative yields within 10 minutes of reaction at a much lower temperature as compared to the reported time of 3- 6 hours via solvent based methods, even in the absence of added catalysts. Thus, a conclusion was drawn from these synthetic experiments that the reaction rates in the case of Imidazole synthesis are amplified not just because of the catalytic effects of added catalysts or *in situ* generated catalysts like acetic acid but also because of the self activation of carbonyls in the condensed phase.

The final part of the work described in the subsection (3.3.3) includes the efficient preparation of a variety of metal complexes of the 2-(4, 5-disubstituted 1H-imidazol-2-yl) phenol. Effective substitution on the diketone and varying the number of metal salts leads to a diversity oriented synthesis of Imidazole metal complexes.

The remarkable versatility and success of using solventless reactions to prepare several classes of compounds demonstrates that this methodology has an important place in the toolbox arsenal for Green Chemistry. In accepting the enormous challenge of Green Chemistry in the march towards sustainability, the results of the work might play a part, whatever miniscule that may be, in encouraging other researchers to draw benefits from this approach vis a vis the classical approach of using volatile organic solvents in synthesis.