Multi-component Synthesis of Some Biologically Active Heterocyclic Compounds

Final Report of

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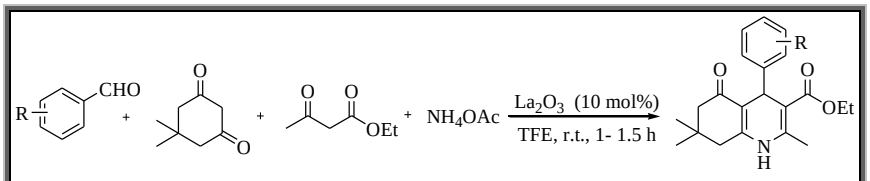
Summary of Findings

Multicomponent reactions (MCR) also referred as the multicomponent assembly processes (MCAP) are the convergent, one-pot reactions of more than two simple precursors. These act as a gateway for providing an easy access to a wide range of functionally novel and complex heterocyclic molecules with high selectivity. MCRs are superior over multistep organic synthesis. During the past decade; MCRs came into light over routine multistep synthesis owing to their atom economy, energy efficiency, lower costs, short reaction time, environmental friendly nature and simpler purification techniques. Such reactions allow the formation of new bonds resulting in diverse molecular complexity in a single step. MCRs play a prominent role in modern drug discovery processes.

Considering the advantages of multicomponent reactions; in the present studies we report the synthesis of following heterocyclic compounds by one-pot multicomponent approach:

- **CHAPTER- I:**

Lanthanum oxide (La_2O_3) was successfully studied as an efficient heterogeneous catalyst for one-pot, four-component synthesis of Hantzsch polyhydroquinoline derivatives from aromatic aldehydes, dimedone, ethyl acetoacetate and ammonium acetate at ambient temperature **(Scheme 1)**. The catalyst is heterogeneous, recyclable and consequently can be easily separated and reused. The present method is featured by mild reaction conditions, use of heterogeneous catalyst, non-chromatographic purification, short reaction time and high yields, which make it an attractive route for the synthesis of polyhydroquinolines.



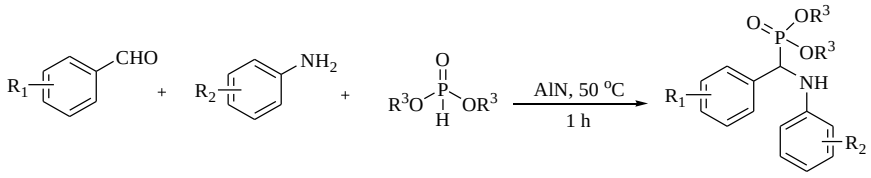
Scheme 1: Synthesis of Hantzsch polyhydroquinoline derivatives by using La_2O_3 / TFE

Publication: *Chin. Chem. Lett.* **2014**, 25, 1149-1152.

- **CHAPTER- 2:**

An important principle of green chemistry is replacing the use of common and hazardous organic solvents needed for chemical transformations. The development of solvent-free multi-component methodologies for the synthesis of heterocyclic compounds has gained tremendous attention of scientific community on account of increasing hazardous effects of volatile organic solvents on the environment and thus become the intensely studied thrust area of research. Solvent-free conditions offer several distinct advantages such as clean reaction profile, enhanced reaction rates, high selectivity and higher yield.

α-Aminophosphonates are the immensely significant bioisosteres of amino acids displaying a broad spectrum of biological applications. In the present studies; some novel α-amino phosphonates were synthesized by the one-pot three-component Kabachnik-Fields reaction involving the condensation of several aromatic aldehydes, amine and dialkylphosphites using aluminium nitride as the reusable heterogeneous catalyst under solvent-free conditions within 1 h reaction time (**Scheme 2**). The synthesized compounds were evaluated for the three types of biological activities i.e. anti-inflammatory, anti-oxidant and cytotoxicity studies. Among these screened compounds; one compound showed promising results.



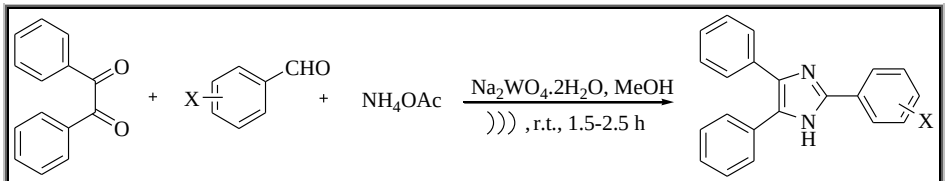
Scheme 2: Synthesis of aminophosphonates by one pot three component Kabachnik - Fields reaction

Publication: *J. Iran. Chem. Soc.* **2014**, *11*, 717-724.

- **CHAPTER-3:**

Ultrasound assisted synthesis of heterocyclic compounds is an escalating application of green chemistry. The technique of using ultrasound for carrying out organic transformations leads to better yields and faster reaction rates under mild temperature conditions.

An environmentally benign ultrasound promoted green one-pot three-component protocol was developed for the synthesis of 2, 4, 5-triaryl substituted imidazoles at room temperature using sodium tungstate dihydrate as a simple and inexpensive catalyst (**Scheme 3**). It constitutes a valuable addition to the existing methods for the synthesis of 2, 4, 5-triaryl substituted imidazoles. This method allowed us to achieve products under ultrasound irradiation in short time and excellent yield without using harmful catalyst.



Scheme 3: Ultrasound promoted sodium tungsate catalyzed synthesis of 2,4,5-triaryl imidazoles

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