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Multicomponent reactions: development, scope, and applications

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Summary

Multi-component reaction (MCR) is a promising synthetic methodology for the rapid and easy access to scaffold with a great diversity and so MCRs find broad applications in pharmaceutical and organic industries. MCRs are considered as ideal reactions due to a wide range of advantages, such as simplicity, high efficiency, green nature, and time efficacy. The finding of new MCRs and their applications to fill chemical space has become an increasingly active area of research.

The research in this thesis is focused on the development of new MCRs and their applications towards generation of biologically important molecules with vast diversity and complexity.

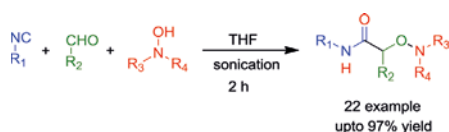
In **Chapter 1**, we give an overview of modern MCRs with a focus on higher MCRs and some intriguing recent applications underscoring the immense potential of navigating the chemical space. Furthermore, the MCRs impact on both drug discovery projects and organic industry are discussed.

In **Chapter 2**, we give an overview of the latest literature covering the Passerini reaction, especially focusing on scope, chirality and applications in diverse areas.

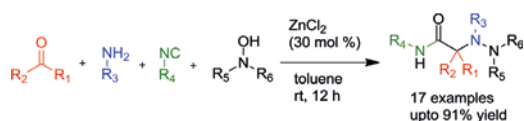
In **Chapter 3**, we describe the new most efficient protocol for the Passerini tetrazole reaction. The scope of the reaction is investigated with various aldehydes and isocyanides.



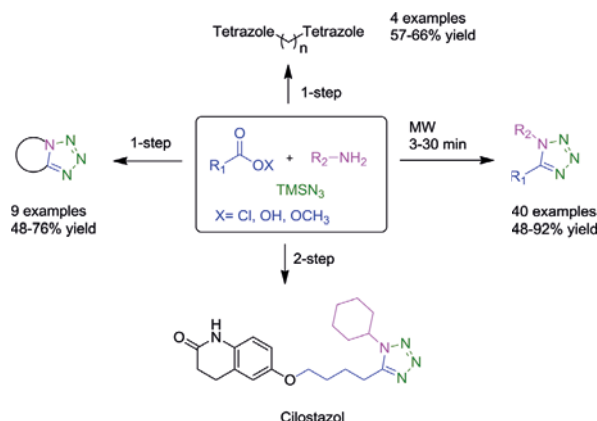
In **Chapter 4**, for the first time N-hydroxamic acid is introduced as an acid isostere in the Passerini multicomponent reaction (P-3CR) towards the one step synthesis of α -aminoxy amide. This sonication-accelerated, catalyst-free, simple, fast and highly efficient Passerini reaction is used for the synthesis of diverse α -aminoxy-amides.



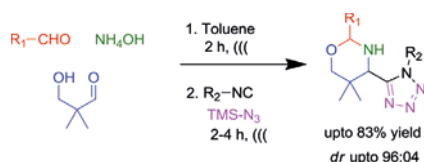
In **Chapter 5**, we describe the successful use of the N-hydroxyimides as an acid isostere in the U-4CR for a direct route to the synthesis of α -hydrazinoamides. This is the first example of cyclic imide migration to nitrogen (O \rightarrow N imide transfer) in the Mumm rearrangement to form an N-N bond.



In **Chapter 6**, we describe the novel microwave accelerated three-component reaction between an amine, a carboxylic acid derivative and an azide source for the construction of the 1,5-tetrazole scaffold. The applications of this method is demonstrated in the synthesis of biologically important fused tetrazole scaffolds and the marketed drug cilostazol.



Chapter 7, is about the union of MCR. We first time used the Asinger-Ugi-tetrazole union for the synthesis of highly diastereoselective 4-(tetrazole)-1,3-oxazinanes. The reaction exhibit excellent diastereoselectivity and broad substrate scope.



In **Chapter 8**, we describe the new $TiCl_4$ -mediated reaction for the direct amination of Passerini-2CR product. This simple, general, additive/base/ligand-free reaction is mediated by economical $TiCl_4$. The validity of this C-N bond formation protocol with diverse amines is discussed.



In **Chapter 9**, we introduced the universal convertible isocyanide in the Ugi-4CR and also in Ugi-tetrazole reaction. The application of this 2-nitro benzyl isocyanide in different reactions and conditions is described.