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Multicomponent reactions: Advanced tools for sustainable synthesis of pharmaceuticals

Romano V A Orru
VU University, The Netherlands

Multicomponent reactions (MCRs) receive increasing attention because they address both diversity and complexity in organic synthesis. With these one-pot reactions diverse sets of relatively complex structures, especially heterocycles, can be generated from simple starting materials. In many MCRs (e.g. the Ugi reaction), isocyanides are important building blocks. Recently, isocyanides have found also application as versatile C1 building block in palladium catalysis. These reactions offer a vast potential for the synthesis of nitrogen containing fine chemicals. In this presentation, the development of novel atom- and step efficient Pd-catalyzed reactions involving isocyanide insertion will be presented. Further, in order to address stereoselectivity issues connected to certain MCRs, biocatalysis offers unique opportunities. Recently, we have developed several methods based on the enzymatic desymmetrization of meso-pyrrolidines using a monoamine oxidase N (MAON) from Aspergillus niger optimized by directed evolution and its combination with highly diastereoselective Ugi-type three-component and Ugi-Smiles reactions. In this presentation we highlight several aspects of this chemistry in the context of heterocycle synthesis with applications in green chemistry and pharmaceuticals.

r.v.a.orru@vu.nl