Multicomponent Reactions

Organic synthesis is the science of making new, unexplored molecules, from simple building blocks to complex products. Exactly this is at the heart of the two *Science of Synthesis* volumes on multicomponent reactions that are the subject of this book review.

Synthetic organic chemistry has evolved at a breathtaking pace over the last two centuries. At the beginning, it was not much more than just mixing different substances, heating, and making a guess as to what molecule might have formed. We have now arrived at a point where it is possible to design a multistep synthesis for almost any conceivable chemical structure, by a rational approach based on the large toolbox of available synthetic methods. Each step of a multistep synthesis involves a chemical reaction. Traditionally, the reagents and conditions for each of the steps should be designed to give a good yield and a pure product, with as little work as possible. To be useful in organic synthesis, a method must be reliable for a broad range of substrates. However, for complex organic molecules, executing such a "total" synthesis is still far from trivial, and is often neither simple nor beautiful. The routes are often lengthy, with many reaction steps employing a multitude of different, sometimes highly creative, protective group strategies and/or using "metal-based" catalysis. The capability for truly sustainable production of complex, highly functionalized molecules for advanced applications as (fine) chemicals and pharmaceuticals, or in food, in materials, or in catalysis, is still far short of maturity. Thus, there is a clear need to discover and develop clean, atom-efficient, and step-efficient one-pot syntheses for sustainable production of molecularly diverse and structurally complex organic molecules with high added-value.

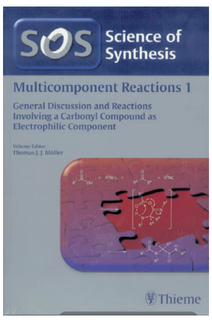
Multicomponent reactions (MCRs) are increasingly valued as efficient synthesis tools to give rapid access to complex products. The two *Science of Synthesis* volumes on multicomponent reactions provide a comprehensive overview of this rapidly evolving field of organic synthesis methodology. With MCRs, molecules can be assembled from three or more starting materials in a one-pot process. MCRs involve the formation of several bonds in a single operation, without the need to isolate the intermediates or to change the reaction conditions, and often without adding further reagents. Therefore, MCRs address sustainability by atom-, step-, and thus eco-efficiency, reducing the number of intermediate steps and functional group manipulations, and avoiding protecting-group strategies. Syntheses involving MCRs save time and energy (step efficiency), and proceed with high convergence (process efficiency). In addition, MCRs are ideally suited for combinatorial chemistry and library design, and are of great utility in medicinal chemistry, materials science, recognition (host–guest) chemistry, and catalyst design. Especially, MCRs can have a crucial role in exploiting the full potential of "diversity-orientated synthesis" (DOS) and "biology-orientated synthesis" (BIOS) design strategies for effective and functional library synthesis, opening up virgin areas of biologically relevant chemical space.

Although the power of MCR chemistry was already recognized in the early days of organic synthesis, many new MCRs have been discovered in the past decade, ranging from relatively straightforward novel 3CRs to a highly complex 8CR. The synthetic chemistry community is indeed now realizing the full potential of MCR-based synthesis.

The editor of these Science of Synthesis volumes on multicomponent reactions, Thomas J. J. Müller, has, with the help of many of the key players in the MCR field, collected together the experimentally most relevant MCR processes to date. The relative reactivities of different functional groups are the key properties for successful MCRs, and this is conceptually outlined and illustrated in a clear and concise manner in the introductory chapters by the volume editor. That is followed by short—but instructive and illustrative—chapters, which describe in great detail the complete range of MCRs that have been developed since the "old" Strecker reaction.

In conclusion, I can fully recommend this reference work to both academic and non-academic researchers who are active in organic synthesis. It can serve as an excellent starting point for their studies of MCR chemistry, or as an entry to the primary MCR literature. The two books contain numerous short chapters that are nicely organized following the general idea of multicomponent reactions, i.e., the successive transformation of reactive functionalities in which the carbonyl group serves a central role. The books demonstrate the enormous potential of MCRs for heterocyclic and medicinal chemistry, and also describe developments outside those traditional areas of application. The different reaction types are nicely covered, including mechanistic details whenever appropriate. The chapters are all supplemented by a large number of detailed and well-selected experimental procedures, which will prove crucial for the reader to quickly start conducting his or her own MCRs.

The presentation of the two volumes shows great care for details, including the authoritative keyword and author indexes and extensive list of abbreviations. The individual chapters have a well-structured layout, and the two volumes as a whole



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are of high quality. Indeed, the sophisticated indexes, with keywords and author names, enable these books to serve as the standard "encyclopedia" on MCR chemistry. Although no collective index is provided (which is perhaps the only minor flaw), this reference work completely covers the current state of the art in MCR synthesis, and offers the reader the quickest and most thorough way to start with MCRs. At the same time, I am convinced that established MCR experts will use it as the reference work of choice. It is a must-have for every chemistry library, and—as the editor states in his introduction—this two volume set on *Multicomponent Reactions* will encourage and stimulate exciting future developments of novel efficient MCRs, to further expand the organic synthesis toolbox and give effective access to natural and non-natural molecular targets of high scientific or economic/societal value.

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