

Preface

Synthetic sophistication has increased to an impressive level in the past two centuries. Ongoing development of novel synthetic concepts and methodologies has opened up the way to the construction of many complex and challenging synthetic targets. However, in spite of its scientific merits and its profound influence on the progress of organic chemistry, it has become clear that much of the present synthetic methodology does not meet the conditions set to future purposes. Increasingly, severe economic and environmental constraints force the synthetic community to think about novel procedures and synthetic concepts to optimize efficiency.

Robotics and combinatorial techniques allow chemists to synthesize single libraries that contain more compounds than ever before. Especially, medicinal chemists but also chemists active in the catalysis area have embraced this efficient new synthesis tool. Moreover, advances in molecular biology and genomics continue to improve our understanding of biological processes and to suggest new approaches to deal with inadequately or untreated diseases that afflict mankind. Despite all the progress in both molecular biology/genomics and combinatorial chemistry methods, it is generally recognized that the number of pharmaceutically relevant hits is not directly proportional to the number of compounds screened. Both structural diversity and complexity in a collection of molecules are essential to address.

Ideally, a synthesis starts from readily available building blocks and proceeds fast and in one simple, safe, environmentally acceptable, and resource-effective operation in quantitative yield. Inspired by Nature, the construction of complex molecules by performing multiple steps in a single operation is receiving considerable attention. Such processes, in which several bonds are formed in one sequence without isolating the intermediates, are commonly referred to as *tandem reactions*. An important subclass of tandem reactions is the multicomponent reactions (MCRs). These are defined as one-pot processes that combine at least three easily accessible components to form a single product, which incorporates essentially all the atoms of the starting materials. MCRs are highly flexible, (chemo)

selective, convergent, and atom-efficient processes of high exploratory power (EN) that minimize solvent consumption and maximize atom efficiency. Many MCRs are well suited for the construction of heterocyclic cores. MCR-based processes therefore contribute to a sustainable use of resources and form the perfect basis for modular reaction sequences comprised of simple reactions that achieve in a minimal number of steps a high degree of both complexity and diversity for a targeted set of scaffolds. As a consequence, the design of novel MCRs and their exploration as tools in especially heterocyclic chemistry receives growing international attention. Novel MCRs are applied in combinatorial and medicinal chemistry but also in catalysis and more traditional natural product syntheses.

These and other topics are at the heart of this volume of *Topics in Heterocyclic Chemistry*, which is entirely devoted to MCRs in the synthesis of heterocycles. This collection of major contributions from established scientists will certainly stimulate discussions and further development in this field of chemistry. I hope that you enjoy it.

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Reactions I

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