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Preface

The length of a synthesis is dependent upon the average molecular complexity produced per operation, which depends in turn on the number of chemical bonds being created. Therefore, devising reactions that achieve multi-bond formation in one operation is becoming one of the major challenges in searching for step-economic syntheses. By today’s standards, besides being regio-, chemo- and stereo-selective, an ideal multi-bond-forming process should satisfy the following additional criteria: (a) readily available starting materials; (b) operationally simple; (c) easily automatable; (d) resource effective (personnel, time, cost etc); (e) atom economical; and (f) ecologically benign. Multicomponent reaction (MCR) processes, in which three or more reactants are combined in a single chemical step to produce products that incorporate substantial portions of all the components, naturally comply with many of these stringent requirements for ideal organic syntheses.

Multicomponent reactions, though fashionable these days, have in fact a long history. Indeed, many important reactions such as the Strecker amino acid synthesis (1850), the Hantsch dihydropyridine synthesis (1882), the Biginelli dihydropyrimidine synthesis (1891), the Mannich reaction (1912), and the isocyanide-based Passerini reactions (1921) and Ugi four-component reactions (Ugi-4CRs) (1959), among others, are all multicomponent in nature. In spite of the significant contribution of MCRs to the state of the art of modern organic chemistry and their potential use in complex organic syntheses, little attention was paid to the development of novel MCRs in the second half of the twentieth century. However, with the introduction of molecular biology and high-throughput biological screening, the demand on the number and the quality of compounds for drug discovery has increased enormously. By virtue of their inherent convergence and high productivity, together with their exploratory and complexity-generating power, MCRs have naturally become a rapidly evolving field of research and have attracted the attention of both academic and industrial scientists.

The development of novel MCRs is an intellectually challenging task since one has to consider not only the reactivity match of the starting materials but also the reactivities of the intermediate molecules generated in situ, their compatibility, and their compartmentalization. With advances in both theory and mechanistic insights into various classic bimolecular reactions that allow for predictive analysis of reaction sequences, the development and control of new reactive chemical