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Domino-Reactions in Natural Product Synthesis and Combinatorial Chemistry

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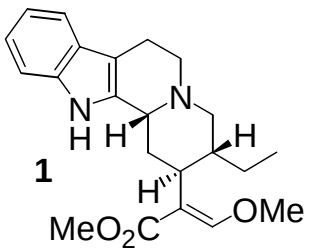
Synthesis of relevant organic compounds such as natural products and analogues, drugs, diagnostics, agrochemicals and any kind of material is a main topic in academic and industrial chemistry. Whereas the race for more selectivity was one of the driving forces in the past - it is still going on - the main goal is now efficiency, the compatibility with our environment, the preservation of our resources and also economical advantages. This new view is clearly a change of paradigm in synthesis. The proportion of the numbers of steps and the increase of complexity is now an important standard for the quality of a synthesis.

A general way to improve synthetic efficiency and also address the above mentioned criteria as well as to give access to a multitude of diversified molecules is the development of domino processes[1-3]. This methodology allows the formation of complex compounds starting from simple substrates in very few steps. We have defined domino reactions as processes of two or more bond forming transformations under widely identical conditions, in which the subsequent reactions take place at the functionalities obtained in the former transformation. Domino processes are also suitability in combinatorial chemistry.



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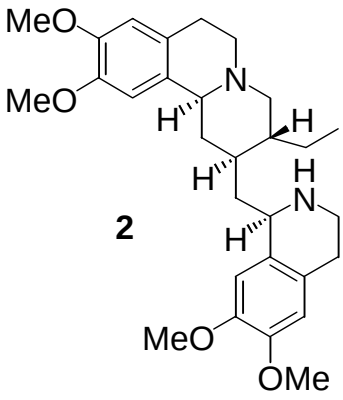

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In my lecture I shall describe the use of domino processes for the efficient enantioselective synthesis of biologically interesting indole, ipecacuanha and erythrina alkaloids [4,5] as e.g. hirsutine **1**[4] and emetine **2**. In addition, two new concepts for combinatorial chemistry will be presented using domino-processes[6].

[1] L. F. Tietze and U. Beifuss, *Angew. Chem.* **1993**, *105*, 137-170; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 131-163. [2] L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115–136. [3] L. F. Tietze, F. Haunert in „Stimulating Concepts in Chemistry“ (Eds. : M. Shibasaki, J. F. Stoddart and F. Vögtle) Wiley VCH, Weinheim **2000**, 39-64. [4] L. F. Tietze, Y. Zhou, *Angew. Chem.* **1999**, *111*, 2076–2078; *Angew. Chem. Int. Ed.* **1999**, *38*, 2045–2047. [5] L. F. Tietze, S. A. A. El Bialy, H. Braun, *Angew. Chem.* **2004**, in press. [6] L. F. Tietze, N. Rackelmann, G. Sekar, *Angew. Chem. Int. Ed. Engl.* **2003**, *42*, 4245-4257.