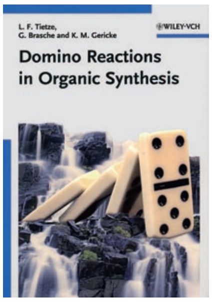
Domino Reactions in Organic Synthesis



By *Lutz F. Tietze*, *Gordon Brasche* and *Kersten M. Gericke*.
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Gigantic domino stones are tumbling down a waterfall. The cover picture of this book reminds one of Goethe's *Italian Voyage* (published in 1829) where, deeply impressed, he describes his visit to the castle park of Caserta on March 14, 1787: "…There an aqueduct funnels a whole stream to water the castle and its surroundings, and the whole masses of water can, if cast onto artificially designed rocks, be transfigured into a most gorgeous cascade…". This moving concert of flowing natural forces, architectural-technical chef d'oeuvre, and aesthetics of design can also be observed in chemical reaction sequences that, after an initiation, proceed in a programmed fashion. They are called domino reactions. Indeed, there are many examples of domino reactions in nature, where cascades of enzyme-catalyzed reactions occur efficiently and selectively, even within the same cell compartment. It is no surprise that Mother Nature was the source of inspiration for this topical modern concept in organic synthesis. In the preface and introduction to this book, the authors make a link between paradigms that is also based on economic and ecological grounds. The emphasis is not on the question of whether a molecule can be synthesized, but rather on how the synthesis is achieved, linking together the fields of domino, multicomponent, and one-pot processes. Professor Tietze and his co-workers are well qualified to present a description and up-to-date snapshot of research on domino reactions. Some ten years ago, a review article with the same title was published by the same senior author. Very soon this review became the lead reference in the field. In view of the breath-taking pace of developments, Tietze and his coworkers now present an excellent overview of this highly topical field, which has opened up new possibilities and potential for further research. Tietze, Brasche, and Gericke have taken on the herculean task of writing a work of 617 pages that aims to give a comprehensive introduction to the use of domino reactions in organic synthesis and a deeper insight into such reactions.

The introduction has to fulfill a vital function. In particular, in this intellectual jungle, where many scientists have mutated into linguistic creators and fantastic neologists, and use terms loosely, the authors of this book begin by stating what domino reactions are and what they are not. Domino reactions are time-resolved transformations, and must be clearly distinguished from simultaneous tandem reactions. The classification of domino reactions is based on reactive organic intermediates and functionalities that occur within the course of a reaction. The different classes are cationic, anionic, free-radical, pericyclic, photochemical, transition-metal-catalyzed, and enzymatic reactions, as well as oxidations and reductions.

The book is clearly structured in ten chapters, with literature references at the end of each chapter. Chapter 1 contains an introduction and description of cationic domino reactions. A description of the rich world of carbenium ion intermediates is followed by polyene cyclizations and rearrangement cascades leading to epoxide transformations, Nazarov cyclizations, and complex polycyclizations terminated by pericyclic processes. As is also the case for all other classes of domino reactions, the clear subcategorization is based on organic reactive properties, which is a thread and leitmotiv of the book.

In the following chapter, anionic intermediates are the carriers of the sequences. Likewise, the addition of an enolate to a Michael system generates the enolate for the subsequent Michael addition. Polycyclic molecules are literally stitched together by anionic species. Familiar reactions such as the aldol reaction are perfectly suited as a final step in a sequence that leads to highly substituted cyclopentanes, beginning with a rhodium-catalyzed Michael addition (Hayashi reaction) of a boronic acid to an α,β-unsaturated carbonyl compound with keto functionality in the side chain. Anionic domino reactions can occur in many combinations, so that the possible subsequent transformations even extend into the realm of transition-metal-catalyzed final steps.

Chapter 3 is dedicated to free-radical domino reactions. During the last few decades, free-radical cyclizations have become an indispensable tool in the nonpolar armory of synthetic chemistry. Many beautiful polycyclizations for the construction of elaborate molecular scaffolds have been successfully applied. As with the preceding types of domino processes, here also the so-called hetero domino reactions come into play. These are combinations of sequences with polar elementary reactions initiated by free-radical steps.

Pericyclic reactions have become popular among synthetic chemists because of their practicability and stereochemical predictability. It is possible to combine many similar or different pericyclic elementary processes to give domino reactions. In many cases they have already found applications in natural product syntheses. They make greater structural complexity possible, and polycyclic structures can be constructed very quickly. The use of Diels–Alder reactions and 1,3-dipolar cycloadditions for initiating programmed sequences literally leads to domino reactions at the push of a button. Sigmatropic rearrangements, electrocyclic reactions, and ene reactions are also mentioned, thus showing that there is an enormous potential for realizing the domino idea.

Chapter 5 also reports a lot of news in the field of photochemically induced domino reactions. The chemistry of the excited state is quite similar to free-radical chemistry, and opens up a wide variety of reactions; these have led to some unusual, mechanistically fascinating, domino sequences for the synthesis of complex structures, as described here by Tietze and co-workers. Photochemically induced cascades followed by metal-catalyzed steps allow catenations of intra- and intermolecular reactions within a single sequence.

In the past three decades, transition-metal catalysis has experienced an enormous boost, and conceptual and strategic thinking in synthesis has been fundamentally revolutionized. Therefore, it is not surprising that this area has produced many new domino reactions. The wonder world of palladium-catalyzed transformations provides the introduction to Chapter 6.

Among palladium-catalyzed reactions, the Heck reaction often plays a key role, in particular because it can be used for multiple insertions of alkenes or alkynes. Besides cross-couplings (Suzuki, Stille, and Sonogashira), transition-metal-catalyzed allylic substitutions have recently received considerable attention as an entry to domino processes. Many rhodium-catalyzed domino sequences are based on the decomposition of diazo compounds followed by in situ generation of 1,3-dipoles. Rhodium-catalyzed hydroformylation also provides an excellent entry to domino reactions, by taking advantage of the aldehyde functionality that is generated. Finally, metathesis and cycloisomerization reactions initiate new types of cascades that often lead to complex polycycles. Almost any transition metal in the Periodic Table can form a basis for surprising selective sequences, so that there are almost no limits to the imagination for chemists seeking new methods.

Domino reactions initiated by oxidation and reduction are introduced in Chapter 7. Changing the oxidation state of functional units in the presence of complementary reactive groups opens the sequence. Particularly advantageous is the existence of highly selective oxidants and reducing agents that commence the sequence under mild reaction conditions. A related concept pursues the in vitro use of enzymes as an entry to domino reactions (Chapter 8). Although nature is the mother of invention of domino processes, this type is particularly suited for the development of designed sequences initiated under physiological conditions to generate highly reactive intermediates.

According to Tietze's definition, a multicomponent reaction is a domino reaction if all components are present in the reaction vessel from the very beginning, and if the conditions are not changed during the course of the reaction. In Chapter 9, this very comprehensive discipline in one-pot methodologies is only treated briefly, but in a condensed and very informative fashion. Historically, many named reactions that are familiar to chemists from introductory lectures in organic chemistry as students belong to this category.

The book ends with an introduction to special techniques in the field of domino reactions (Chapter 10). These include domino processes under high pressure, on solid supports, without solvents, or accelerated by microwave radiation. There is no doubt that the future holds prospects for further techniques and methodologies that will find entry to highly efficient processes such as domino reactions.

In all chapters, the authors have also described a lot of very recent research. The most recent references belong to the summer of 2005, and even some examples from 2006 are included as "last-minute" illustrations, which emphasizes that this is a dynamic and highly topical field of research. Overall, the book adds up to an excellent presentation of a fascinating area of science. Only one minor point of criticism must be mentioned: the large number of reaction schemes shown has led to a few mistakes, which should have been detected by a conscientious proofreader. These mistakes are not misleading or serious, but they could have been avoided. However, this does not diminish the value of the book at all.

In conclusion, the book gives a felicitous introduction and an accurate up-to-date picture of the world of domino reactions and their applications in organic synthesis. It can be recommended to novices and adepts, students and researchers, in both academia and industry, as an outstanding, easy to read, lead reference.

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