

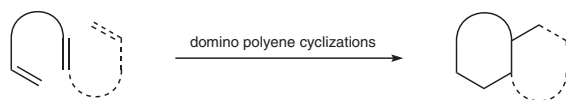
Abstracts

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1.1 Polyene Cyclizations

R. A. Shenvi and K. K. Wan

A domino transformation consists of a first chemical reaction enabling a second reaction, which can then effect a third reaction, and so on, all under the same reaction conditions. A polyene cyclization is defined as a reaction between two or more double bonds contained within the same molecule to form one or more rings via one or more C–C bond-forming events. Herein, domino polyene cyclizations are discussed, with an emphasis on operationally simple methods of broad utility. From the perspective of synthesis theory, polyene cyclizations are a powerful approach for the efficient generation of both complexity and diversity, with the potential for a single synthetic route to generate a series of both constitutional and stereochemical isomers. However, with some noteworthy exceptions, the ability to controllably cyclize a linear chain to multiple products with high selectivity still generally eludes synthetic chemists and represents a significant chemical frontier for further development.



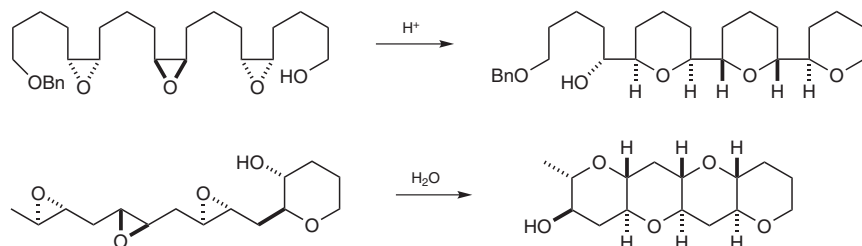
Keywords: polyenes · cyclization · carbocations · radicals · polycycles

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1.2 Cation- π Cyclizations of Epoxides and Polyepoxides

K. W. Armbrust, T. Halkina, E. H. Kelley, S. Sittihan, and T. F. Jamison

This chapter describes the formation of complex polycyclic fragments from linear epoxide and polyepoxide precursors via domino reactions. Depending on the reaction conditions employed, either *exo* or *endo* epoxide opening can be selectively achieved. Applications of these domino reactions toward the synthesis of complex natural products are discussed.

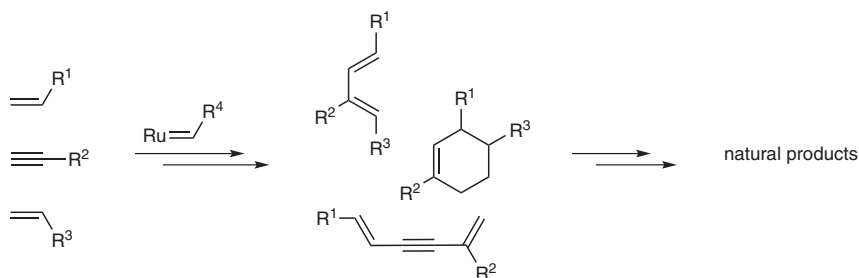


Keywords: oxiranes · cascades · natural products · marine ladder polyethers · ionophores · ethers · oxygen heterocycles · tetrahydrofurans · tetrahydropyrans · oxepanes

1.3.1 Enyne-Metathesis-Based Domino Reactions in Natural Product Synthesis

D. Lee and M. O'Connor

Enyne-metathesis-based domino processes are highlighted in the context of natural product synthesis; these include domino double ring-closing metathesis, enyne metathesis/metallo-tropic [1,3]-shifts, enyne metathesis/Diels–Alder reaction, and other variations of their domino combinations. Issues regarding selectivity and mechanism are also discussed.

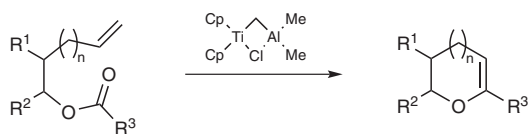


Keywords: enyne metathesis • π -bond exchange • domino transformations • natural products • total synthesis

1.3.2 Domino Metathesis Reactions Involving Carbonyls

H. Renata and K. M. Engle

This review describes different methods to perform net carbonyl–alkene metathesis. Reactions of this type generally involve domino transformations employing organometallic reagents. Different conditions and procedures are surveyed and strategic applications of carbonyl–alkene metathesis in the synthesis of natural products are highlighted.

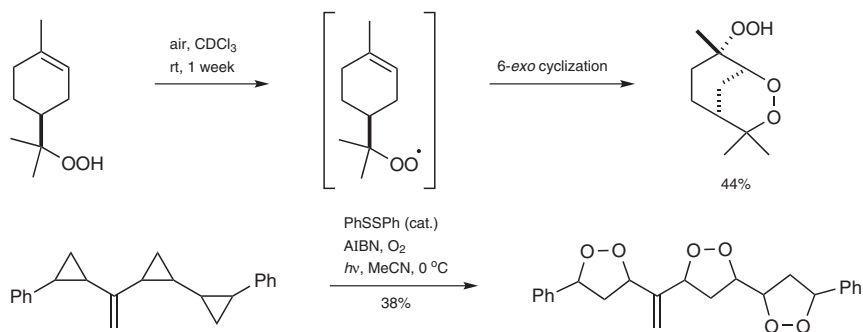


Keywords: metathesis • alkenylation • carbonyl compounds • alkenes • ring closure • transition metals • titanium complexes • organometallic reagents • organocatalysts

1.4.1 Peroxy Radical Additions

X. Hu and T. J. Maimone

In this chapter, radical addition reactions involving peroxy radical intermediates are reviewed. These transformations typically generate a carbon radical intermediate which then reacts with molecular oxygen forming a peroxy radical species. Following peroxy radical cyclization, various endoperoxide rings are constructed. Two major classes of reactions are discussed: (1) radical additions to alkenes and quenching with molecular oxygen, and (2) radical formation from the opening of cyclopropanes and incorporation of molecular oxygen. Various methods for radical initiation that are compatible with the presence of molecular oxygen are described.



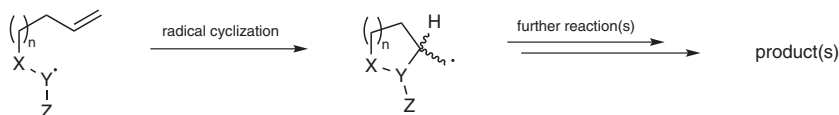
Keywords: peroxide synthesis · endoperoxides · cyclic peroxides · radical addition · peroxy radicals · thiyl radicals · hydroperoxidation · cyclopropane cleavage · 1,2-dioxolanes · 1,2-dioxanes · 1,2-dioxepanes

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1.4.2 Radical Cyclizations

J. J. Devery, III, J. J. Douglas, and C. R. J. Stephenson

This chapter details recent examples of domino radical reactions that are initiated via an intramolecular radical cyclization.



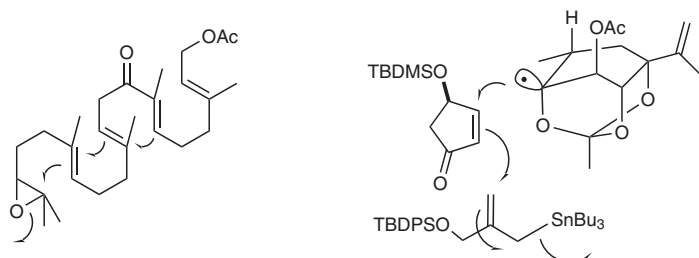
Keywords: radicals · domino reactions · cyclization · tin · samarium · organo-SOMO · ammonium cerium(IV) nitrate (CAN) · visible light

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1.4.3 Tandem Radical Processes

K. A. Parker

This review presents selected examples of regio- and stereospecific domino radical reactions developed in the context of total synthesis studies. The underlying strategies demonstrate the variety of connectivity patterns that can be generated by cascades of intra- and intermolecular bond-forming steps.

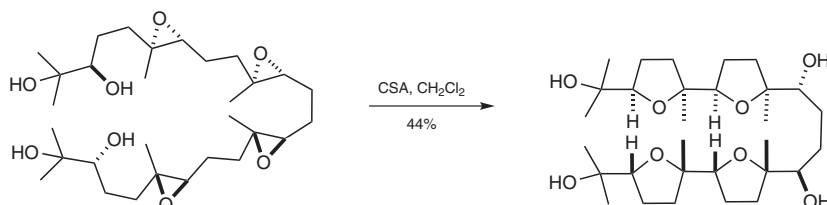


Keywords: tandem radical cyclization · radical domino cyclization · radical cascade cyclization · intermolecular reactions · radical trapping · manganese(III) acetate · titanocene dichloride · tris(trimethylsilyl)silane · triethylborane · tri-*sec*-butylborane · TEMPO · 1,1,3,3-tetramethylguanidine · samarium(II) iodide · cobaloxime

1.5.1 Protic Acid/Base Induced Reactions

D. Adu-Ampratwum and C. J. Forsyth

This chapter covers synthetic domino processes that are induced by protic acid or base. They are broadly classified into those that capitalize upon the release of oxirane ring strain under acidic or basic conditions, and carbocyclic ring expansions and contractions under protic acid or basic conditions. The focus here is upon single substrate, monocomponent domino processes, rather than multicomponent variants.

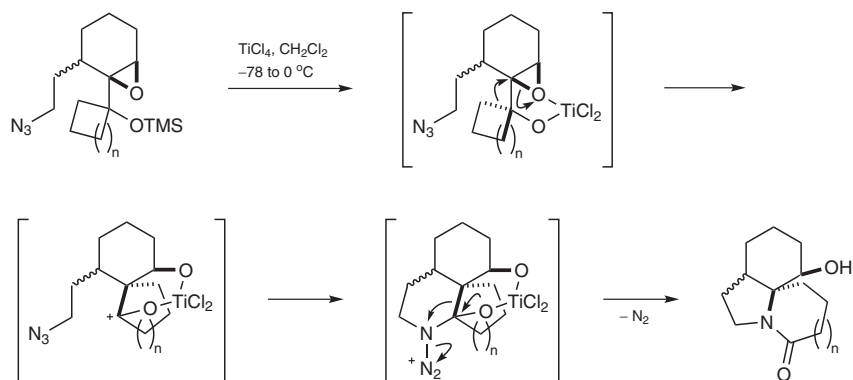


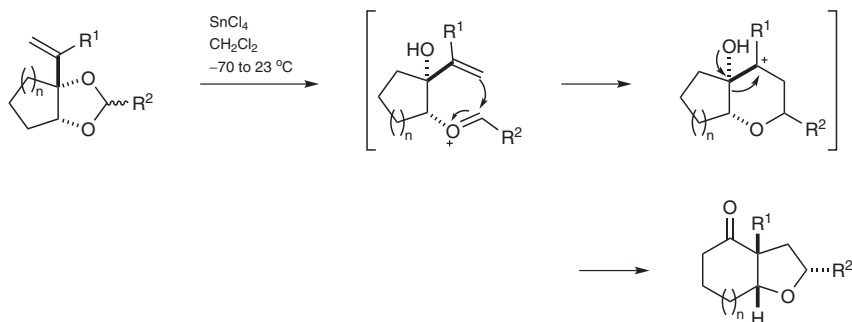
Keywords: carbocyclic compounds • cyclization • epoxy compounds • ethers • Favorskii rearrangement • intramolecular reactions • Nazarov cyclization • pinacol rearrangement • ring contraction • ring expansion • tandem reactions • Wagner–Meerwein rearrangement

1.5.2 Lewis Acid/Base Induced Reactions

S.-H. Wang, Y.-Q. Tu, and M. Tang

The efficient construction of complex molecular skeletons is always a hot topic in organic synthesis, especially in the field of natural product synthesis, where many cyclic structural motifs can be found. Under the assiduous efforts of synthetic chemists, more and more methodologies are being developed to achieve the construction of cyclic skeletons. In particular, the beauty and high efficiency of organic synthesis are expressed vividly among those transformations realized through a domino strategy. Based on these important methodologies, selected Lewis acid/base induced domino reactions leading to ring expansions, contractions, and closures are presented in this chapter.





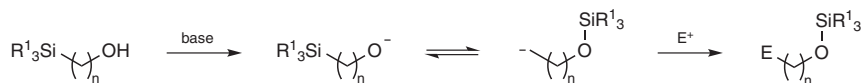
Keywords: tandem reactions • Lewis acid • Lewis base • ring expansion • ring contraction • ring closure

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1.5.3 Brook Rearrangement as the Key Step in Domino Reactions

A. Kirschning, F. Gille, and M. Wollig

The Brook rearrangement has lost its Cinderella status over the past twenty years since being embedded into cascade reaction sequences. The powerful formation of carbanions through silyl migration has been exploited for the development of many new methodologies and has been used as a key transformation in complex natural product syntheses. Now, the Brook rearrangement belongs to the common repertoire of synthetic organic chemists.



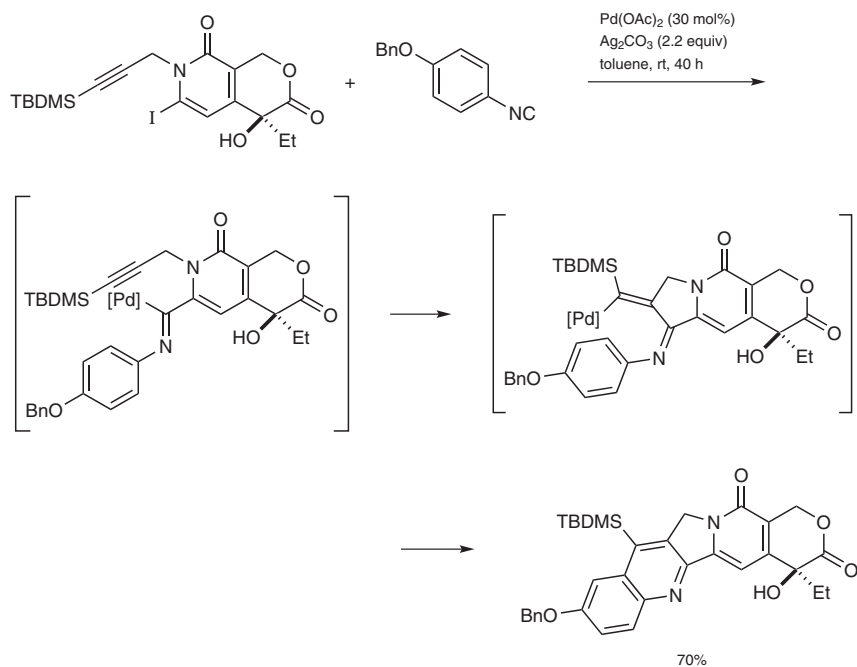
Keywords: Brook rearrangement • domino reactions • migration • organosilicon chemistry • total synthesis

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1.6.1 Palladium-Mediated Domino Reactions

E. A. Anderson

Palladium catalysis offers excellent opportunities to engineer domino reactions, due to the ability of this transition metal to engage with a variety of electrophiles and to effect stereocontrolled bond formations in complex settings. This review covers palladium-catalyzed domino processes, categorized according to the initiating species (alkenyl-, aryl-, allyl-, allenyl-, or alkylpalladium complexes), with a particular focus on applications in natural product synthesis that exemplify more general methodology.

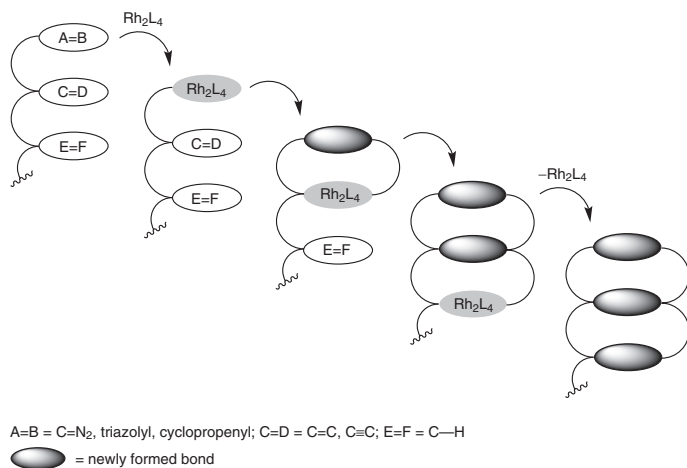


Keywords: palladium · domino · cascade · total synthesis

1.6.2 Dirhodium-Catalyzed Domino Reactions

X. Xu, P. Truong, and M. P. Doyle

With dirhodium carbenes generated from diazocarbonyl compounds, 1-sulfonyl-1,2,3-triazoles, or cyclopropenes, a subsequent intramolecular cyclization forms a reactive intermediate that undergoes a further transformation that usually terminates the reaction process. Commonly, the electrophilic dirhodium carbene adds intramolecularly to a $\text{C}\equiv\text{C}$ bond to provide a second rhodium carbene. Catalytically generated dirhodium-bound nitrenes initiate domino reactions analogously, and recent examples (nitrene to carbene to product) have also been documented.



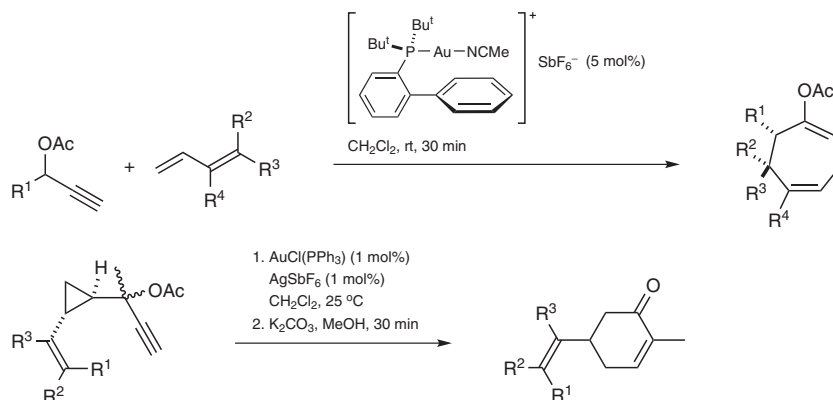
Keywords: α -carbonyl carbenes · (azavinyl)carbenes · cyclopropenes · [3 + 2] annulation · cyclopropenation · carbene/alkyne metathesis · carbonyl ylide reactions · Claisen/Cope rearrangement · C–H insertion · oxonium ylides · dipolar cycloaddition · aromatic substitution

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1.6.3 Gold-Mediated Reactions

E. Merino, A. Salvador, and C. Nevado

In this review, a selection of the most relevant examples featuring gold-catalyzed domino transformations are presented. Processes catalyzed by both gold(I) and gold(III) complexes are described, including multicomponent reactions, annulations, cycloisomerizations, and cycloadditions. The scope, limitations, and mechanistic rationalization of these transformations are also provided.



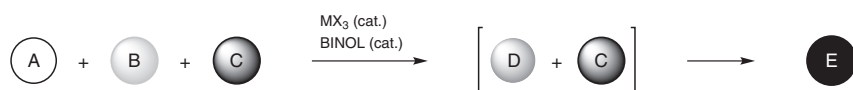
Keywords: domino transformations · multicomponent reactions · cycloisomerizations · cycloadditions · rearrangements · gold

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1.6.4 Rare Earth Metal Mediated Domino Reactions

T. Ohshima

Rare earth metals, comprising 17 chemical elements in the periodic table, are relatively abundant in the Earth's crust despite their name. In the series of lanthanides, a systematic contraction of the ionic radii is observed when going from lanthanum to lutetium (often referred to as the lanthanide contraction), but this variation is so smooth and limited, with ca. 1% contraction between two successive lanthanides, that it is possible to fine-tune the ionic radii, Lewis acidity, and Brønsted basicity of rare earth complexes. As a result of the large size of the lanthanide ions compared to other metal ions, lanthanide ions have high coordination numbers, varying from 6 to 12. Due to the strong oxophilicity of rare earth elements, their metal ions have a hard Lewis acidic nature. Most particularly, rare earth metal trifluoromethanesulfonates [M(OTf)₃] have been regarded as new types of Lewis acids and are stable and active in the presence of many Lewis bases. Another important type of rare earth metal species, the rare earth metal alkoxides [M(OR)₃], exhibit both Lewis acidity and Brønsted basicity. These collated characteristic features of rare earth based complexes, such as high coordination numbers, a hard Lewis acidic nature, high compatibility with various functional groups, ease of fine-tuning, and multifunctionality, have led to the development of a variety of domino reactions catalyzed largely by rare earth metal trifluoromethanesulfonates and alkoxides.



M = rare earth metal; X = OTf, OR¹

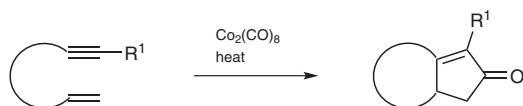
Keywords: lanthanide contraction • rare earth metal trifluoromethanesulfonates • rare earth metal alkoxides • Lewis acidity • Brønsted basicity • high coordination numbers • multifunctionality

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1.6.5 Cobalt and Other Metal Mediated Domino Reactions: The Pauson–Khand Reaction and Its Use in Natural Product Total Synthesis

L. Shi and Z. Yang

The Pauson–Khand reaction constitutes one of the most formidable additions to the repertoire of synthetically useful reactions. It rapidly affords a cyclopentenone skeleton from an alkene, an alkyne, and carbon monoxide, based on a domino sequence of bond constructions. In this chapter, the prowess of the Pauson–Khand reaction is illustrated by judicious selection of complex target molecules, the total syntheses of which are cleverly orchestrated by the key Pauson–Khand reaction sequence. Emphasis is placed on cobalt-mediated processes to exemplify the applicability of this classical reaction.



Keywords: Pauson–Khand reaction • alkenes • carbon monoxide • alkynes • cyclopentenones • natural product synthesis • octacarbonyldicobalt • thioureas • allenic alkynes • asymmetric synthesis