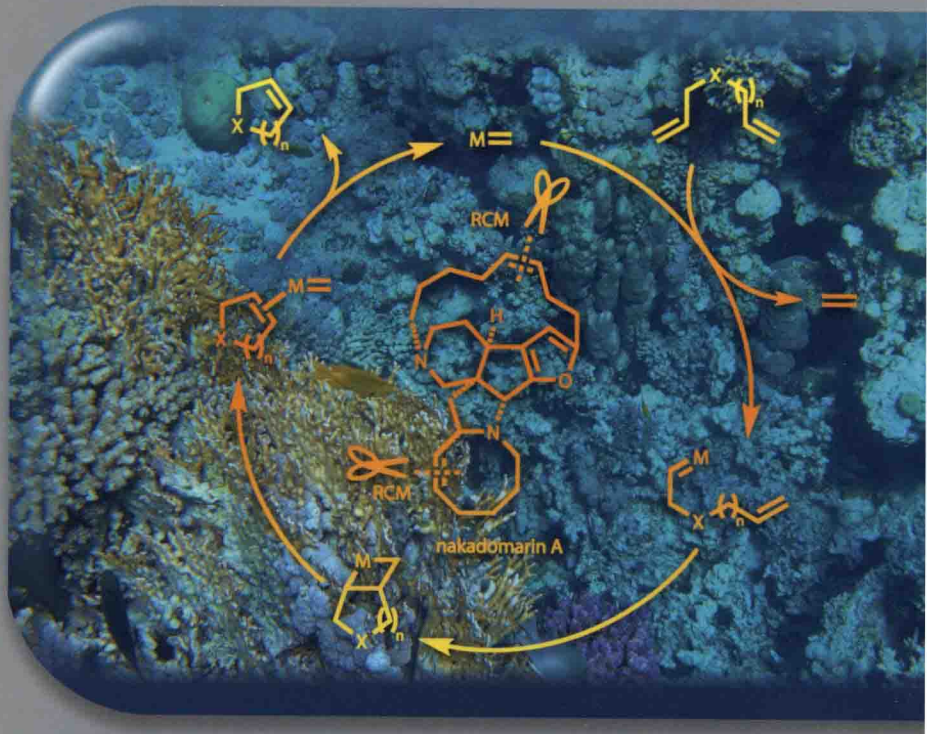
Science of Synthesis

Metal-Catalyzed Cyclization Reactions 1

Volume Editors
Shengming Ma
Shuanhu Gao



Thieme

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Volume Editors **S. Ma**
S. Gao

Authors
J. M. Alderson
E. M. Beccalli
A. Bonetti
S. Gao
P. J. Guiry
S. Jammi
A. Mazza
C. Nottingham
A. M. Phelps
J. M. Schomaker
M. Shi
X. Tang
D. Wang
Y. Yamamoto
S.-L. You
L. Zhang
X. Zhang

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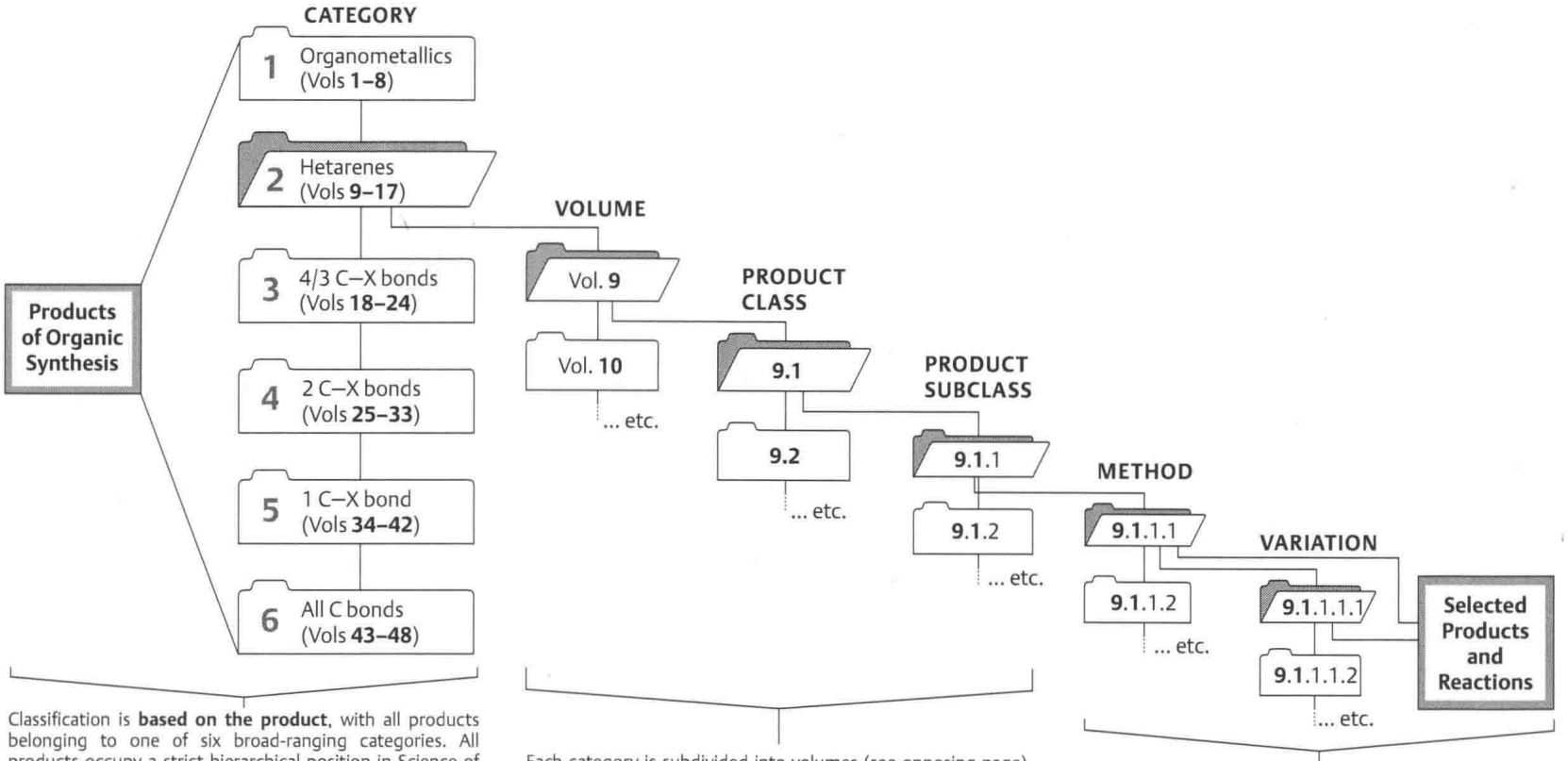
Organizational Structure of Science of Synthesis*

* A complete description of the full classification principles can be found in the **Science of Synthesis Guidebook.**



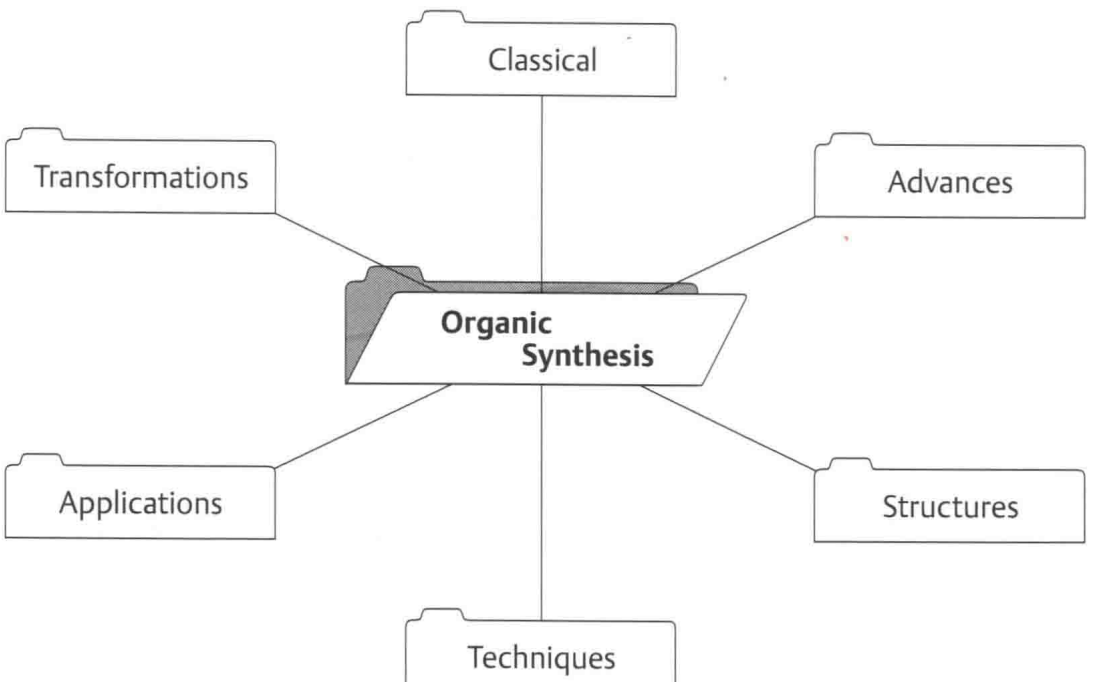
Classification is **based on the product**, with all products belonging to one of six broad-ranging categories. All products occupy a strict hierarchical position in Science of Synthesis, defined according to the classification principles*. Products in Categories 3–6 are organized according to oxidation state, with products containing the greatest number of carbon–heteroatom (C—X) or C—C π-bonds to a single carbon occupying the highest positions (e.g., carboxylates, enolates, and alcoholates are covered in Categories 3, 4, and 5, respectively).

Each category is subdivided into volumes (see opposing page), each of which is devoted to discrete groupings of compounds called **product classes** (e.g., "Thiophenes" is Product Class 10 of Volume 9). Product classes may be further subdivided into **product subclasses**, (e.g., "Thiophene 1,1-Dioxides" is Product Subclass 3 of Product Class 10 of Volume 9). Consequently, the relationship between heading name and heading number varies below product class level within individual volumes.

For each product class or subclass, a number of methods are described for synthesizing the general product type. Often there are variations on a method given. Both methods and variations contain experimental procedures with relevant background information and literature references. **Selected products and reactions** display the scope and limitations of the methods.

Science of Synthesis Reference Library

The **Science of Synthesis Reference Library** comprises volumes covering special topics of organic chemistry in a modular fashion, with six main classifications: (1) Classical, (2) Advances, (3) Transformations, (4) Applications, (5) Structures, and (6) Techniques. Volumes in the **Science of Synthesis Reference Library** focus on subjects of particular current interest with content that is evaluated by experts in their field. **Science of Synthesis**, including the **Knowledge Updates** and the **Reference Library**, is the complete information source for the modern synthetic chemist.



Science of Synthesis

Science of Synthesis is the authoritative and comprehensive reference work for the entire field of organic and organometallic synthesis.

Science of Synthesis presents the important synthetic methods for all classes of compounds and includes:

- Methods critically evaluated by leading scientists
- Background information and detailed experimental procedures
- Schemes and tables which illustrate the reaction scope

Science of Synthesis

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Preface

As the pace and breadth of research intensifies, organic synthesis is playing an increasingly central role in the discovery process within all imaginable areas of science: from pharmaceuticals, agrochemicals, and materials science to areas of biology and physics, the most impactful investigations are becoming more and more molecular. As an enabling science, synthetic organic chemistry is uniquely poised to provide access to compounds with exciting and valuable new properties. Organic molecules of extreme complexity can, given expert knowledge, be prepared with exquisite efficiency and selectivity, allowing virtually any phenomenon to be probed at levels never before imagined. With ready access to materials of remarkable structural diversity, critical studies can be conducted that reveal the intimate workings of chemical, biological, or physical processes with stunning detail.

The sheer variety of chemical structural space required for these investigations and the design elements necessary to assemble molecular targets of increasing intricacy place extraordinary demands on the individual synthetic methods used. They must be robust and provide reliably high yields on both small and large scales, have broad applicability, and exhibit high selectivity. Increasingly, synthetic approaches to organic molecules must take into account environmental sustainability. Thus, atom economy and the overall environmental impact of the transformations are taking on increased importance.

The need to provide a dependable source of information on evaluated synthetic methods in organic chemistry embracing these characteristics was first acknowledged over 100 years ago, when the highly regarded reference source **Houben–Weyl Methoden der Organischen Chemie** was first introduced. Recognizing the necessity to provide a modernized, comprehensive, and critical assessment of synthetic organic chemistry, in 2000 Thieme launched **Science of Synthesis, Houben–Weyl Methods of Molecular Transformations**. This effort, assembled by almost 1000 leading experts from both industry and academia, provides a balanced and critical analysis of the entire literature from the early 1800s until the year of publication. The accompanying online version of **Science of Synthesis** provides text, structure, substructure, and reaction searching capabilities by a powerful, yet easy-to-use, intuitive interface.

From 2010 onward, **Science of Synthesis** is being updated quarterly with high-quality content via **Science of Synthesis Knowledge Updates**. The goal of the **Science of Synthesis Knowledge Updates** is to provide a continuous review of the field of synthetic organic chemistry, with an eye toward evaluating and analyzing significant new developments in synthetic methods. A list of stringent criteria for inclusion of each synthetic transformation ensures that only the best and most reliable synthetic methods are incorporated. These efforts guarantee that **Science of Synthesis** will continue to be the most up-to-date electronic database available for the documentation of validated synthetic methods.

Also from 2010, **Science of Synthesis** includes the **Science of Synthesis Reference Library**, comprising volumes covering special topics of organic chemistry in a modular fashion, with six main classifications: (1) Classical, (2) Advances, (3) Transformations, (4) Applications, (5) Structures, and (6) Techniques. Titles will include *Stereoselective Synthesis*, *Water in Organic Synthesis*, and *Asymmetric Organocatalysis*, among others. With expert-evaluated content focusing on subjects of particular current interest, the **Science of Synthesis Reference Library** complements the **Science of Synthesis Knowledge Updates**, to make **Science of Synthesis** the complete information source for the modern synthetic chemist.

The overarching goal of the **Science of Synthesis** Editorial Board is to make the suite of **Science of Synthesis** resources the first and foremost focal point for critically evaluated information on chemical transformations for those individuals involved in the design and construction of organic molecules.

Throughout the years, the chemical community has benefited tremendously from the outstanding contribution of hundreds of highly dedicated expert authors who have devoted their energies and intellectual capital to these projects. We thank all of these individuals for the heroic efforts they have made throughout the entire publication process to make **Science of Synthesis** a reference work of the highest integrity and quality.

The Editorial Board July 2010

Science of Synthesis Reference Library

Metal-Catalyzed Cyclization Reactions (2 Vols.)
Applications of Domino Transformations in Organic Synthesis (2 Vols.)
Catalytic Transformations via C—H Activation (2 Vols.)
Biocatalysis in Organic Synthesis (3 Vols.)
C-1 Building Blocks in Organic Synthesis (2 Vols.)
Multicomponent Reactions (2 Vols.)
Cross Coupling and Heck-Type Reactions (3 Vols.)
Water in Organic Synthesis
Asymmetric Organocatalysis (2 Vols.)
Stereoselective Synthesis (3 Vols.)

Volume Editors' Preface

Metal-catalyzed reactions, especially cyclizations, remain the most useful methods for the efficient construction of cyclic compounds and thus have continuously attracted attention. These methodologies have also been comprehensively applied as the key steps in various novel strategies for the synthesis of natural products and drug molecules. Many new discoveries and advances have been reported, which provide new tools for synthetic organic chemists, medicinal chemists, and even materials chemists. A timely summary is now required of the well-established advances that will shape the future development of this field and its application. On the basis of these considerations, the Editorial Board of *Science of Synthesis* planned two volumes in the Reference Library that focus on metal-catalyzed cyclization reactions. After a careful selection made by the Volume Editors, some of the most significant and practical metal-catalyzed reactions for modern organic synthesis are presented. The organization of these two volumes is based on the types of reaction, which mainly include metal-catalyzed C—C, C—O, and C—N bond formations, as well as epoxidation, aziridination, cyclopropanation, Pauson–Khand reactions, cycloadditions, radical reactions, and metathesis. We hope that these volumes can serve as a reference work for chemists in related areas to inspire future research and the development of new applications.

We would like to take this opportunity to express our sincere thanks for the support and contributions from all of the outstanding authors; without their dedication and professionalism, this project would not have been possible. We are also grateful to Alex Russell and Joe P. Richmond, scientific editors at *Science of Synthesis*, who solved a lot of problems to enable the project to proceed smoothly over the past two and a half years. It has been a very pleasant journey to work with the editorial team at Thieme, especially Michaela Frey and Guido F. Herrmann. We appreciate the professional spirit and passion of all members of this team, which have brought the manuscripts together into a two-volume set.

Volume Editors

Shengming Ma and Shuanhu Gao

Shanghai, May 2016

Abstracts

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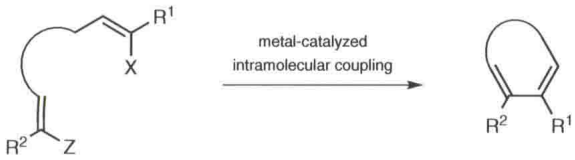
1.1 Metal-Catalyzed Intramolecular Coupling Reactions

S. Gao and D. Wang

This chapter presents metal-catalyzed or -promoted intramolecular cross-coupling reactions for C—C bond formation in the preparation of cyclic compounds. Examples of synthetic applications in natural products syntheses are discussed to illustrate the potential of these methodologies.



Keywords: cross coupling · reductive coupling · intramolecular coupling · C—C bond formation · palladium · chromium · copper · nickel · Suzuki–Miyaura coupling · Stille coupling · Negishi coupling · Sonogashira coupling · Hiyama coupling · dehydrogenative coupling · Nozaki–Hiyama–Kishi coupling · ene–yne coupling

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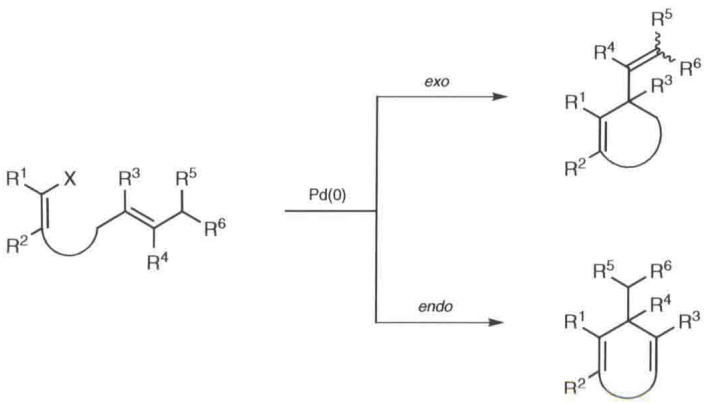
1.2 Intramolecular Heck Reactions

S. Jammi, C. Nottingham, and P. J. Guiry

This chapter presents the best methods for non-enantioselective and enantioselective intramolecular Heck reactions to form cyclic molecules.



Keywords: intramolecular Heck cyclization · non-enantioselective · enantioselective · chiral · cross coupling · palladium(0) · halide · pseudohalide · alkene

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1.3 Metal-Catalyzed Intramolecular Allylic Substitution Reactions

X. Zhang and S.-L. You

Metal-catalyzed intramolecular allylic substitution reactions provide diverse carbocycles and heterocycles. Various types of nucleophiles such as carbon, nitrogen, and oxygen can be employed.

LG = leaving group; Nu = C, N, O

Keywords: allylic substitution · amines · gold · indoles · intramolecular reactions · iridium · palladium · phenols · ruthenium

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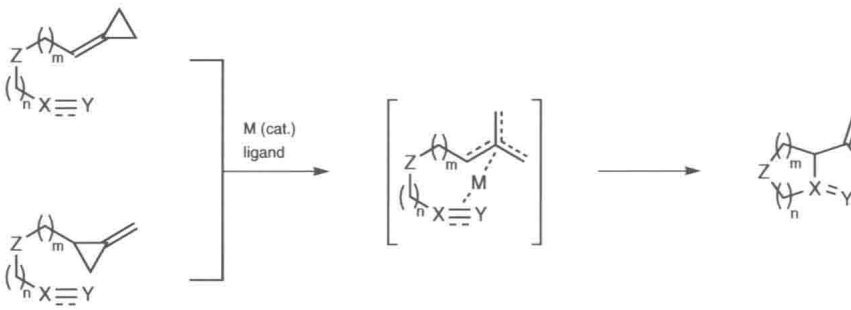
1.4 Metal-Catalyzed Intramolecular Cyclizations Involving Cyclopropane and Cyclopropene Ring Opening

X. Tang and M. Shi

Due to the ring strain of cyclopropane rings, transition-metal catalysts can easily undergo an oxidative addition with the cyclopropane moiety of methylenecyclopropanes (MCPs) to give trimethylenemethane (TMM) intermediates. Subsequent intramolecular cyclization with unsaturated systems takes place to give cyclized products. Moreover, in the presence of a chiral ligand, high enantioselectivity can be achieved. The ring-fused products are versatile building blocks in organic synthesis.



Z = O, CR^1R^2, NR^1; n = m = 0, 1, 2; M = Pd, Ni, Rh, Ru

Keywords: cyclopropanes · methylenecyclopropanes · ring-opening reactions · cyclization · alkenes · alkynes · transition-metal catalysts · trimethylenemethanes · palladium · nickel · rhodium · ruthenium · chiral synthesis