Cross Coupling and Heck-Type Reactions 3

Metal-Catalyzed Heck-Type Reactions and C–C Cross Coupling via C–H Activation

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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
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.

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

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I am delighted to present this new volume in the Science of Synthesis Reference Library series addressing metal-catalyzed Heck-type reactions and C—C cross coupling via C—H activation. The formation of C—C bonds is of paramount importance in organic synthesis and has captured the attention of organic chemists since the very beginning of modern synthetic chemistry. Transition-metal-catalyzed coupling, and especially palladium-catalyzed coupling, has emerged as an efficient and selective method for the arylation and vinylation of a range of different substrates. Amongst the palladium-catalyzed couplings, the Heck reaction (or the Mizoroki–Heck reaction) is one of the most prominent examples. This was recently recognized by the Royal Swedish Academy of Sciences, who jointly awarded Richard F. Heck, Ei-ichi Negishi, and Akira Suzuki the 2010 Nobel Prize in Chemistry.

This volume provides comprehensive coverage of the different classes of Heck-type reactions. It describes the latest state-of-the-art developments in each area whilst critically evaluating the strengths and weaknesses of the different methods. In accordance with the growing demand for synthetic efficiency and practicality in organic synthesis, many of these newly developed Heck-type methods feature operationally convenient conditions, high catalytic efficiency, and high levels of chemical, regiochemical, and stereochemical control. Metal-catalyzed C—H functionalization has also been developed into a powerful tool for organic synthesis, providing for original C—C disconnections in retrosynthetic analysis and improving the overall efficiency of the desired transformations. This volume also summarizes the most important concepts and methods in this hot research area.

The different chapters have, in all cases, been authored by respected researchers active in the field. Of interest to both academic and industrial chemists, the introductory overview on each class of transformation is followed by presentation of the most important methods that have been developed, including experimental procedures. It is with satisfaction that I have observed the increased use of, and interest in, metal-catalyzed Heck-type reactions and C—H couplings over the last decade. I hope that this volume will appeal not only to experts in homogeneous catalysis but also to a broader group of organic and medicinal chemists, both in universities and in the pharmaceutical and related industries. I believe that this volume reflects the relevance and timeliness of the subject matter and will enhance current efforts to expand the scope and application of these powerful transformations.

I would like to take this opportunity to express my sincere gratitude to all the authors of this volume and thank them for their careful and comprehensive work. Furthermore, I would like to thank Associate Editor Dr Luke R. Odell, not only for his skilled efforts and concise work during the difficult process of editing and proofing the complete volume, but also for his highly valuable help to all of us who write in English but not as our first language. I also wish to express my appreciation to the outstanding staff at Thieme, in particular Dr. M. Fiona Shortt de Hernandez, Dr. Matthew Weston, and Ms. Michaela Frey, for their highly valuable help in preparing yet another timely volume in the Science of Synthesis Reference Library series.

M. Larhed (Uppsala, Sweden)  October, 2012
Cross Coupling and Heck-Type Reactions Volumes

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Metal-Catalyzed Heck-Type Reactions and C—C Cross Coupling via C—H Activation
Volume Editor: M. Larhed
Abstracts

3.1.1.1 Reaction with Aryl or Hetaryl Halides or Pseudohalides
C.-M. Andersson and M. Andersson

The arylation of terminal alkenes bearing mesomerically electron-withdrawing groups is the archetypal palladium(0)-catalyzed Heck reaction, also known as the Mizoroki–Heck reaction. These substrates generally provide a very high regioselectivity, with both steric and electronic factors favoring arylation at the terminal position of the alkene. Additionally, diastereoselectivity is generally very high, and products with an E configuration are obtained exclusively in most cases. In the wake of the pioneering studies on this reaction in which stoichiometric amounts of palladium reagents were used, iodoarenes were introduced as arylating agents in a catalytic version of the reaction; these were later supplemented by bromo- and chloroarenes. Subsequently, many other arylating agents, such as pseudohalides, aryl chlorides, and diazonium or iodonium salts, have been introduced as electrophiles in the Mizoroki–Heck reaction. Later advances include the development of oxidative Heck arylations catalyzed by palladium(II) species.

This chapter aims to provide a general perspective on the applicability of this type of coupling chemistry, and to describe the depth and breadth of various aspects that have been researched and refined in making the Heck reaction of alkenes bearing electron-withdrawing groups a cornerstone of the art of C–C bond formation.

Ar1 = aryl, hetaryl; X = I, Br, Cl, N2+; I′Ar2, OTf;
EWG = COR1, CO2R1, CN, CONHR1, SOR1, SO2R1, SO3R1, S(O)OR1, P(O)(OR1)2, PR1(O)OR2, NO2, NO, CZnH3−n (Z = halogen), aryl, hetaryl

Keywords: arylation • electron-poor alkenes • catalysis • palladium • Heck reaction • Mizoroki–Heck reaction • alkenylation • aryl halides • oxidative arylation • aryloboronic acids • iodonium salts • diazonium salts • aryl trifluoromethanesulfonates • ionic liquids

3.1.1.2 Reaction with (Het)Arylmetals or (Het)Arenes
E. W. Werner and M. S. Sigman

The intermolecular Heck reaction, in which a vinylic C–H bond is replaced by a C–C bond under palladium catalysis, is an indispensable tool for synthetic organic chemists. The reasons for this reliance include predictable regioselectivity in the formation of the new C–C bond when electronically biased alkenes are used, and the dependable delivery of configurationally pure E-alkene products. When palladium(II) salts are employed as catalysts in conjunction with organometallic reagents, an external oxidant is required to render the reaction catalytic. This strategy enables the reaction to perform well under mild conditions as compared to the elevated temperatures typically required when using palladium(0) catalysts. A critical review of the reagents and conditions capable of performing such transformations upon electron-deficient alkene substrates is presented.
This chapter presents the synthesis of aryl-substituted alkenes via transition-metal-catalyzed decarbonylative, decarboxylative, or desulfinylative Mizoroki–Heck cross-coupling reactions.

Keywords: alkenes • arylation • cross-coupling reactions • decarbonylation • decarboxylation • desulfinylation • Heck reaction • palladium catalysis • rhodium catalysis • transition-metal catalysis

The Heck reaction is a widely used method in organic synthesis. This report concerns the development of methodologies to apply Heck-type chemistry to electron-poor alkenes with one or more electron-withdrawing groups and alkenyl and other nonaromatic electrophiles.

Keywords: acrylates • alkenes • alkenylation • benzylations • catalysts • $C\equiv C$ bonds • $C-C$ coupling • cross-coupling reactions • dienes • enols • Heck reaction • iodonium compounds • oxidative addition • palladium catalysts • palladium complexes • phosphates • styrenes • sulfonates • vinyl compounds

The intermolecular coupling of aryl or vinyl halides (or pseudohalides) with linear alkenes having an allylic or homallylic heteroatomic substituent occurs under palladi-