

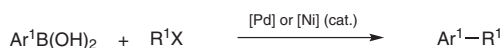
Abstracts

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1.1.1.1 Arylboronic Acid Cross-Coupling Reactions

A. S. Guram, J. E. Milne, J. S. Tedrow, and S. D. Walker

The use of arylboronic acids as coupling partners in metal-catalyzed C–C bond-forming processes has become a mainstay in organic synthesis. These ubiquitous reagents are used across a variety of fields including pharmaceutical, agrochemical, fine chemical, and materials research. This chapter provides a review of the use of arylboronic acids in both traditional cross-coupling reactions and oxidative cross-coupling reactions. The examples presented have been selected with the practicing chemist in mind, and are intended to highlight particularly practical, general, and efficient methods. For large-scale applications, process robustness, catalyst cost and recovery, as well as removal of residual metal from the reaction product are significant considerations that are discussed when possible.



R¹ = aryl, hetaryl, vinyl, acyl, benzyl, alkyl, alkynyl

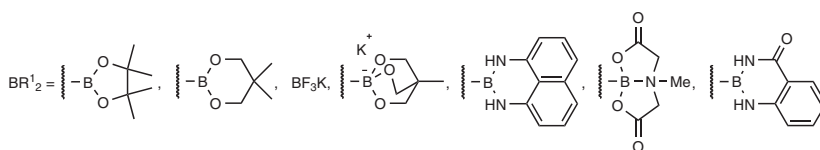
Keywords: arylboronic acids • cross-coupling reactions • oxidative cross-coupling reactions • Suzuki–Miyaura coupling • palladium catalysts • nickel catalysts • phosphine ligands • N-heterocyclic carbene ligands • biaryls

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1.1.1.2 Arylboronic Acid Derivative Cross-Coupling Reactions

M. Suginome and T. Ohmura

The use of arylboronic acid derivatives, not including the parent arylboronic acids, in Suzuki–Miyaura coupling is described in this chapter. Reaction examples using pinacol esters of arylboronic acid are provided with respect to coupling with aryl, alkenyl, and alkyl halides and pseudohalides. Typical reaction conditions as well as exclusive uses in large-ring formation and polycondensation are demonstrated. Recent interesting reactions using an arylboronic ester derived from 2,2-dimethylpropane-1,3-diol are also described. Unique reactivities of aryltrifluoroborates and aryltriolborates are covered in this chapter. Organoboron compounds derived from naphthalene-1,8-diamine (DAN), *N*-methyliminodiacetic acid (MIDA), and anthranilamide (AAM) are also highlighted. The boronyl groups of these compounds are masked or protected under Suzuki–Miyaura coupling conditions. Synthetic applications of these masked boron reagents in iterative Suzuki–Miyaura coupling and C–H functionalization are demonstrated.

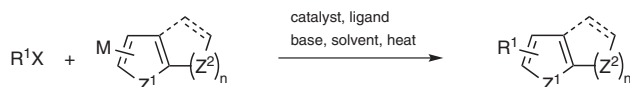


Keywords: biaryls • borates • boron compounds • cross-coupling reactions • iterative coupling • palladium catalysts • Suzuki–Miyaura polycondensation

1.1.2 Hetarylboron Cross-Coupling Reactions

A. Littke

This chapter concerns the Suzuki coupling of hetarylboronic acids or their derivatives (such as boronate esters or potassium trifluoroborates) with electrophiles under either nickel or palladium catalysis. The electrophiles are predominantly aryl or hetaryl halides or pseudohalides (e.g., trifluoromethanesulfonates, methanesulfonates, or 4-toluenesulfonates), although this is not exclusively the case. The chapter is arranged according to the hetarylboronic acid/acid derivative used and, since it is quite difficult to select one method as best for any given acid/electrophile pairing, several methods are presented for each subchapter based on generality, substrate scope, and yield. More modern methods, developed in the context of activating typically reticent aryl chlorides, feature extensively throughout the chapter, and frequently utilize bulky, electron-rich phosphine ligands. However, older methods that feature “traditional” triarylphosphine ligands have not been ignored when these methods can reasonably be anticipated to work well for certain substrates, such as more reactive aryl iodides and bromides. In order to aid the chemist in identifying and selecting the most promising reaction conditions for a given Suzuki coupling, tables are included for certain subchapters whereby further reaction details, substrate pairs, and functional groups are presented. Finally, a representative experimental procedure has been included for each subchapter, which is typically taken from one of the more general methods under discussion. With very few exceptions, all of the methods and procedures presented feature chemistry that, although potentially air- and moisture-sensitive, does not require the use of a glovebox or any special apparatus or experimental techniques.



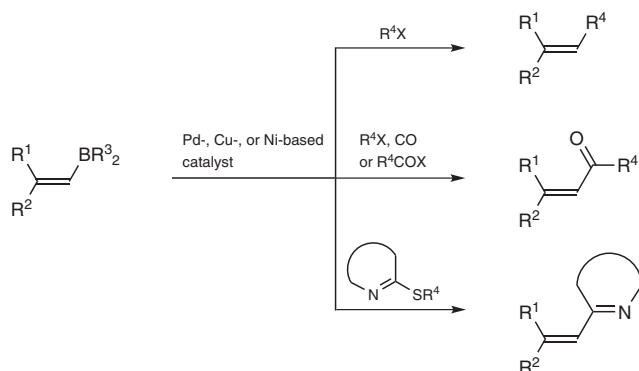
R¹ = aryl, hetaryl, vinyl, etc.; X = I, Br, Cl, OTf, etc.; Z¹ = N, O, S; Z² = C, N, O, S;
n = 1, 2, etc.; M = B(OH)₂, B(OR²)₂, BF₃K, etc.

Keywords: benzofurans · benzothiophenes · furans · hetarylboronic acids · imidazoles · indoles · isoquinolines · isoxazoles · nickel catalysis · oxazoles · palladium catalysis · phosphine ligands · pinacolboronates · pyrazines · pyrazoles · pyridazines · pyridines · pyrimidines · pyrroles · quinolines · Suzuki coupling · thiazoles · thiophenes · trifluoroborate salts

1.1.3 Alkenylboron Cross-Coupling Reactions

B. Carboni and F. Carreaux

Due to their configurational stability, the preservation of the stereochemical integrity in the final product, and their compatibility with a broad range of functional groups, alkenyl organoboranes are key reagents in metal-mediated cross-coupling reactions. A wide variety of alk-1-enyl, benzyl, alkyl, alk-1-ynyl, aryl, and hetaryl halides have been utilized as electrophiles with various organoboron species. Carbonylative coupling, acylation reactions, and desulfinate and desulfonylative couplings are also discussed in this chapter.



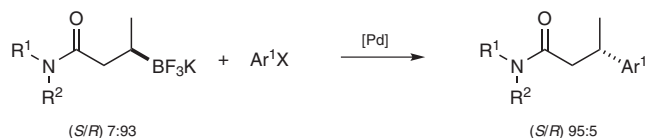
Keywords: transition-metal catalysis · boronic acids · boronic esters · organotrifluoroborates · alkenes · dienes · enynes · carbonylative coupling · desulfinative and desulfonylative coupling

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1.1.4 Alkylboron Cross-Coupling Reactions

D. L. Sandrock

Alkylboron reagents have emerged as useful nucleophilic partners for the installation of alkyl groups onto preexisting molecular scaffolds. The preference for using boron as opposed to other metals is a result of the high air and moisture stability, as well as the functional group tolerance, that organoboron derivatives provide. This chapter presents an overview of the classes of alkylboron reagents that can be employed as the nucleophilic partner in palladium-catalyzed cross-coupling reactions. Specifically, this chapter is organized by the nature of the organic group that is bound to the boron.



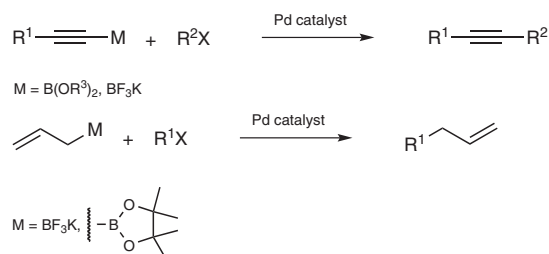
Keywords: alkylboranes · alkylboronates · alkylboronic acids · alkylboron reagents · alkyltrifluoroborates · palladium catalysis · Suzuki–Miyaura cross coupling

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1.1.5 Alkynyl- and Allylboron Cross-Coupling Reactions

F. Colobert and F. R. Leroux

This chapter describes the cross coupling of alkynyl- and allylboron reagents with aryl, alkenyl, and allyl electrophiles. It focuses on the literature published since 1995. These reactions lead to the regioselective formation of new C–C bonds.



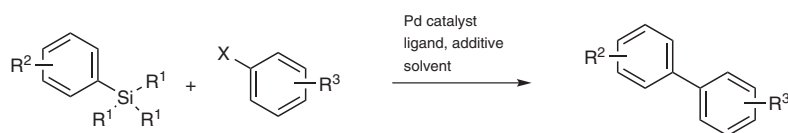
Keywords: alkynylboron · allylboron · cross coupling · palladium · platinum · nickel · copper

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1.2.1 Arylsilicon Cross-Coupling Reactions

S. Denmark and W.-T. T. Chang

Organosilanes have emerged as viable alternatives to the conventional boron, tin, and zinc reagents employed for palladium-catalyzed cross-coupling reactions. Silicon-based reagents possess the added benefits of low cost, low toxicity, and high chemical stability. In contrast to the boron- and tin-based reagents, the diversity of silicon-based reagents that undergo successful cross coupling is enormous. This chapter presents a thorough overview of the combinations of aromatic transferable groups and organic electrophiles. The scope of the coverage is limited to the combination of silicon-bearing nucleophiles with halo or related electrophiles under catalysis by palladium or nickel complexes wherein the silyl halide (or pseudohalide) is lost. The chapter is organized according to the nature of the silicon moiety to which the transferable group is attached.



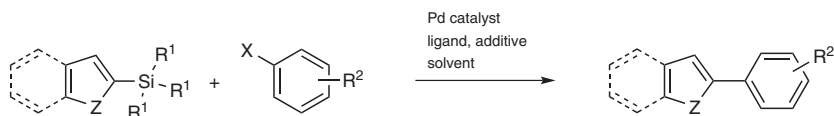
Keywords: cross coupling · organosilicon compounds · arylsilanes · halosilanes · silanols · silanolates · alkoxyasilanes · palladium · ligands · fluoride · mechanisms · enantioselectivity

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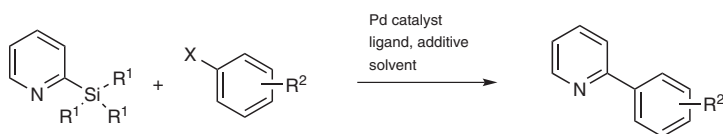
1.2.2 Hetarylsilicon Cross-Coupling Reactions

S. Denmark and W.-T. T. Chang

Organosilanes have emerged as viable alternatives to the conventional boron, tin, and zinc reagents employed for palladium-catalyzed cross-coupling reactions. Silicon-based reagents possess the added benefits of low cost, low toxicity, and high chemical stability. In contrast to the boron- and tin-based reagents, the diversity of silicon-based reagents that undergo successful cross coupling is enormous. This chapter presents a thorough overview of the combinations of heteroaromatic transferable groups and organic electrophiles. The scope of the coverage is limited to the combination of silicon-bearing nucleophiles with halo or related electrophiles under catalysis by palladium or nickel complexes wherein the silyl halide (or pseudohalide) is lost. The chapter is organized according to the nature of the silicon moiety to which the transferable group is attached.



Z = NR³, O, S

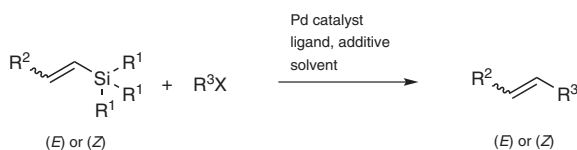


Keywords: cross coupling · organosilicon compounds · hetarylsilanes · silanols · silanolates · alkoxyasilanes · palladium · ligands · fluoride

1.2.3 Alkenylsilicon Cross-Coupling Reactions

S. Denmark and W.-T. T. Chang

Organosilanes have emerged as viable alternatives to the conventional boron, tin, and zinc reagents employed for palladium-catalyzed cross-coupling reactions. Silicon-based reagents possess the added benefits of low cost, low toxicity, and high chemical stability. In contrast to the boron- and tin-based reagents, the diversity of silicon-based reagents that undergo successful cross coupling is enormous. This chapter presents a thorough overview of the combinations of alkenyl transferable groups and organic electrophiles. The scope of the coverage is limited to the combination of silicon-bearing nucleophiles with halo or related electrophiles under catalysis by palladium or nickel complexes wherein the silyl halide (or pseudohalide) is lost. The chapter is organized according to the nature of the silicon moiety to which the transferable group is attached. Selected illustrations of the application of silicon-based cross-coupling reactions as key steps in the total synthesis of natural products are provided.



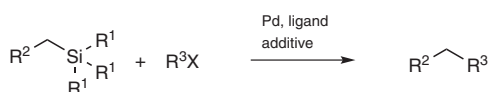
R³ = aryl, alkenyl

Keywords: cross coupling · organosilicon compounds · alkenylsilanes · halosilanes · silanols · silanolates · alkoxysilanes · polysiloxanes · disiloxanes · cyclic silyl ethers · palladium · ligands · fluoride · mechanisms · *cine* rearrangement · stereospecificity

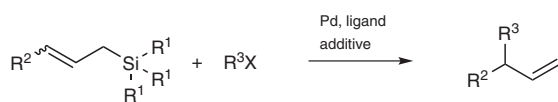
1.2.4 Alkylsilicon Cross-Coupling Reactions

S. Denmark and W.-T. T. Chang

Organosilanes have emerged as viable alternatives to the conventional boron, tin, and zinc reagents employed for palladium-catalyzed cross-coupling reactions. Silicon-based reagents possess the added benefits of low cost, low toxicity, and high chemical stability. In contrast to the boron- and tin-based reagents, the diversity of silicon-based reagents that undergo successful cross coupling is enormous. This chapter presents an overview of the combinations of alkyl transferable groups and organic electrophiles. Alkyl groups include allyl and benzyl groups. The scope of the coverage is limited to the combination of silicon-bearing nucleophiles with halo or related electrophiles under catalysis by palladium or nickel complexes wherein the silyl halide (or pseudohalide) is lost. The chapter is organized according to the nature of the silicon moiety to which the transferable group is attached.



R³ = aryl, alkenyl



$\text{R}^2 = \text{H, Me}; \text{R}^3 = \text{aryl, alkenyl}$

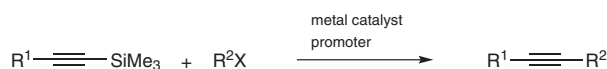
Keywords: cross coupling · organosilicon compounds · alkylsilanes · allylsilanes · benzylsilanes · fluorosilanes · silanols · silanolates · palladium ligands · fluoride · mechanisms · stereospecificity

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1.2.5 Alkynyl- and Acylsilicon Cross-Coupling Reactions

A. Chartoire and S. P. Nolan

This chapter highlights the different strategies described in the literature for the cross coupling of alkynyl- and acylsilicon derivatives with electrophiles. The various methodologies are classified according to the metal catalyst and the promoters used for the transformations.



metal = Pd, Cu, Ag; promoter = F^- , base, solvent

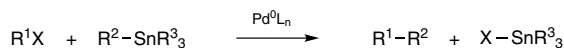
Keywords: cross coupling · alkynylsilicon · palladium · fluoride · silver · copper

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1.3.1 Organotin Cross-Coupling Reactions

A. Pitaval and A. M. Echavarren

This chapter covers organotin cross-coupling reactions, with an emphasis on the most significant progress made over the last decade in the Stille coupling reactions involving a wide variety of organic electrophiles, from traditional substrates such as alkenyl and aryl halides to the less reactive alkyl halides. Significant advances include the use of copper salts as cocatalysts and the introduction of bulky phosphines and other ligands that favor formation of more reactive, coordinatively unsaturated palladium species. The most relevant studies carried out to determine the various mechanisms of the Stille reaction are also reviewed.



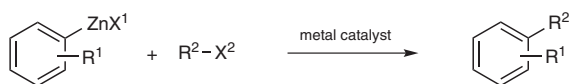
Keywords: Stille coupling · stannanes · cross-coupling reactions · palladium catalysts · copper catalysts · phosphines · transmetalation · oxidative addition · reductive elimination · organic electrophiles · sulfonates

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1.4.1 Arylzinc Cross-Coupling Reactions

C. Gosmini and M. Corpet

This chapter describes different methods for C—C bond formation by cross coupling of arylzinc compounds with various electrophiles in the presence of transition-metal catalysts. The functional group tolerance of these methods means that diverse and functionalized compounds can be synthesized.



R² = aryl, hetaryl, alkyl, alkenyl, acyl, alkynyl; metal = Pd, Ni, Co, Cu, Fe, Rh

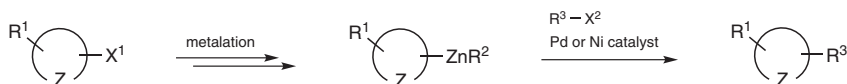
Keywords: arylzincs · catalysis · cross coupling · transition metals · biaryls · styrenes · diarylmethanes · aromatic ketones

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1.4.2 Hetarylzinc Cross-Coupling Reactions

K. Undheim

Cross-coupling reactions with C–C bond formation are effected from hetarylzinc reagents and organo halides, or less commonly from the corresponding organo sulfonate or phosphorus-derived esters. The coupling reactions are promoted by palladium or nickel catalytic systems. The hetarylzinc reagents for the Negishi reaction are available after a metal insertion reaction into a carbon–halogen bond, a C–H bond, or a C–O bond in a regio- and/or chemoselective manner. Zincated reagents can be prepared directly in this manner. Lithium or magnesium reagents available by this procedure are transzincated, commonly by means of a zinc halide, before the Negishi coupling reaction. The introduction of a carbon substituent onto a hetarene substrate under the Negishi conditions is usually a high-yielding process.



Z = N, O, S, X¹ = H, halogen; R² = halogen, hetaryl; X² = halogen, SR⁴, OSO₂R⁴

Keywords: Negishi reactions · C–C bond formation · cross coupling · palladium catalysis · nickel catalysis · metalation · hetaryllithium · hetarylmagnesium · hetarylzinc

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1.4.3 Alkenylzinc Cross-Coupling Reactions

T. Mejuch and I. Marek

Alkenylzinc reagents are broadly applied in various cross-coupling reactions. As they are nowadays easily accessible and because they possess good reactivity and functional group tolerance, alkenylzinc species have become very useful coupling partners. Metal-catalyzed cross-coupling reactions of such reagents with various sp³, sp², and sp electrophiles have been performed as a part of a range of synthetic transformations, including syntheses of natural products.



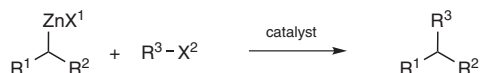
R⁴ = alkyl, alkenyl, aryl, alkynyl

Keywords: alkenylation · alkenylzinc reagents · alkynes · C–C coupling · C=C bonds · vinylmetal species · palladium catalysis

1.4.4 Alkylzinc Cross-Coupling Reactions

L. Li and M. R. Biscoe

Alkylzinc nucleophiles undergo cross-coupling reactions with carbon electrophiles in the presence of transition-metal catalysts. Efficient procedures for cross coupling of primary and secondary alkylzinc reagents with aryl, hetaryl, alkenyl, and alkyl electrophiles are described.



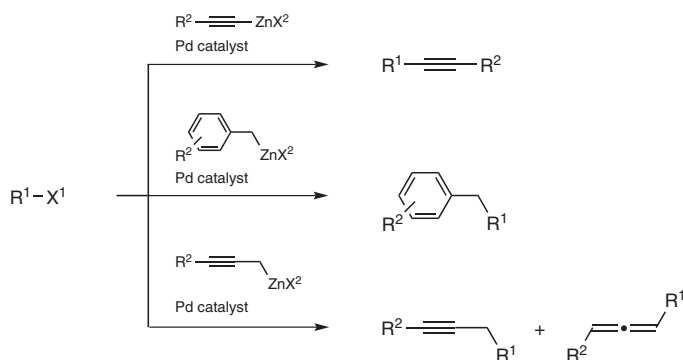
R³ = aryl, hetaryl, alkenyl, alkyl

Keywords: cross-coupling reactions · C–C coupling · Negishi coupling · arylation · alkylation · alkylzinc reagents · palladium catalysts · nickel catalysts · alkyl halides

1.4.5 Alkynyl-, Benzyl-, and Propargylzinc Cross-Coupling Reactions

I. J. S. Fairlamb and A. R. Kapdi

Cross-coupling reactions involving the use of alkynylmetal reagents are of considerable interest. Their applications range from the preparation of simple synthetic intermediates to therapeutic compounds, biologically active natural products, molecular wires and switches, especially “push-pull” systems. Alkynylzinc reagents comprise one such class, which can provide superior product yields and improved reaction rates in comparison with other alkynylmetals. In this review, standard procedures for the synthesis of alkynylzinc reagents (as well as benzylic and propargylic zinc reagents) and their applications in cross-coupling reactions with various electrophilic partners are presented.



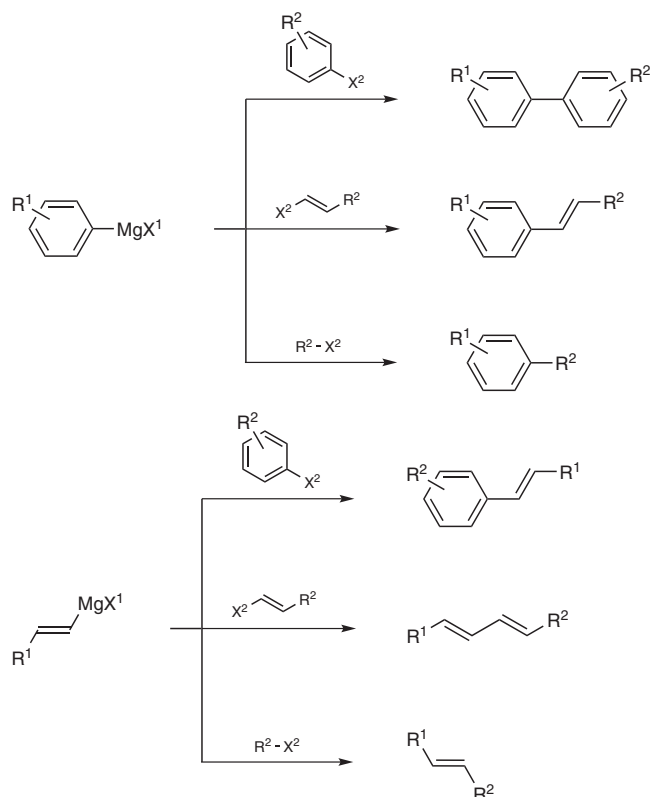
Keywords: alkynylmetals · organozinc reagents · alkynylzinc reagents · Negishi coupling · benzylzinc reagents · propargylzinc reagents · arylalkynes · palladium catalysis

1.5.1 Aryl-, Hetaryl-, and Alkenylmagnesium Cross-Coupling Reactions

C. Wolf

The cross coupling of aryl-, hetaryl-, and alkenylmagnesium reagents with aryl, hetaryl, alkenyl, alkynyl, and alkyl electrophiles provides an increasingly attractive means for efficient C–C bond formation. The direct use of Grignard reagents is generally economically more attractive than Stille, Suzuki, or Negishi coupling reactions, which require an extra step for the synthesis of the tin, boron, or zinc species, respectively. The introduction

of mild protocols for the formation of organomagnesium compounds and the development of effective catalysts that favor C–C bond formation over β -hydride elimination have significantly extended the use of Grignard reagents in cross coupling. Many protocols utilize mild reaction conditions and tolerate a wide range of functional groups.



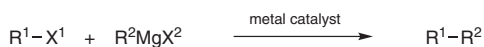
Keywords: Grignard reagents • cross coupling • C–C bond formation • oxidative addition • transmetalation • reductive elimination • isomerization • β -hydride elimination • arylation • alkenylation • alkynylation • alkylation • functional group tolerance • chiral biaryls • atroposelective biaryl formation • enantiotoposelective synthesis

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1.5.2 Alkyl- and Alkynylmagnesium Cross-Coupling Reactions

K. Park and H. Jo

This chapter reviews the transition-metal-catalyzed cross-coupling reactions of alkyl and alkynyl Grignard reagents with alkenyl, aryl, and alkyl electrophiles. The focus is on nickel-, palladium-, iron-, and cobalt-catalyzed processes.



R^1 = alkyl, alkenyl, aryl, hetaryl; R^2 = alkyl, alkynyl;
 X^1 = halogen, OTf, OTs, OC(O)NR³₂, OP(O)(OR³)₂, SO₂OR³;
 X^2 = Cl, Br, I; metal = Ni, Pd, Fe, Co

Keywords: alkyl Grignard reagents • alkynyl Grignard reagents • C–C coupling • cross-coupling reactions • transition metals