

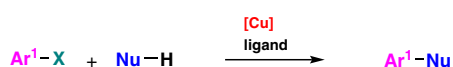
## Abstracts

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### 1.1 Modern Ullmann-Type Couplings

*J. Huang*  and *D. Ma* 

Ligand-promoted, copper-catalyzed, Ullmann-type couplings of aryl halides (I, Br, Cl) with various nucleophiles, including amines, hetarenes, amides, hydrazines, alcohols, phenols, thiols, sulfinates, and active methylene compounds, are reviewed in this chapter. Considerable attention has been paid to demonstrate the powerful acceleration effect of second-generation oxalic amides as ligands in modern Ullmann-type couplings. Under these catalyst systems, less-reactive but inexpensive (het)aryl chlorides can be employed as coupling partners. Moreover, the catalyst loading for coupling of aryl iodides and bromides can be reduced to <1 mol% in most cases.



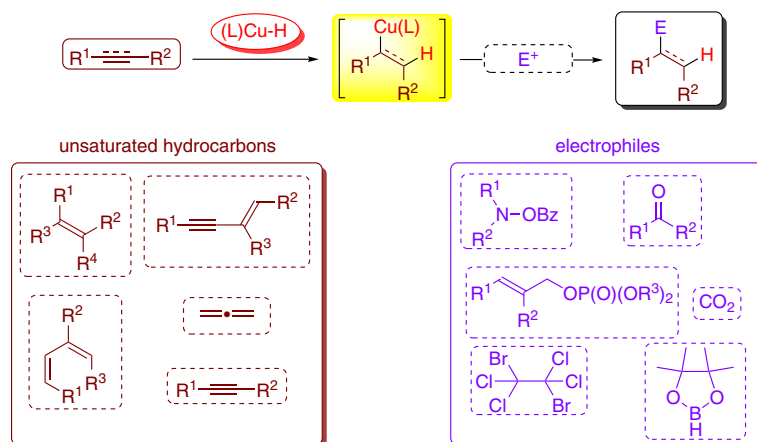
Ar<sup>1</sup> = aryl, hetaryl; X = I, Br, Cl; Nu = [C], [N], [O], [S], [P]

**Keywords:** oxalic amides · amino acids · diamines · copper catalysts · acceleration effect · cross coupling · aryl halides · amines · hetarenes · alcohols · phenols · thiols · sulfinates · active methylene compounds

## 1.2 Copper(I) Hydride Catalyzed Transformations

T. Xiong<sup>1b</sup> and Y. Li

Copper(I) hydride is a binary metal hydride that, due to the relatively low electropositivity of copper, features a rather covalent metal–hydrogen bond. This readily obtained species can either be pre-prepared or generated in situ, and reacts with various unsaturated bonds or polar single bonds to form intermediates with reactive C–Cu bonds, which can be captured by various electrophiles to form new chemical bonds and new stereocenters. In this chapter, some representative examples in this domain are discussed, with the methods divided into four sections based on the different kinds of electrophiles. The first three sections cover asymmetric C–N, C–C, and C–B bond formation with various electrophilic nitrogen sources, carbon-based reagents, and boranes, and the last section focuses on some racemic transformations.

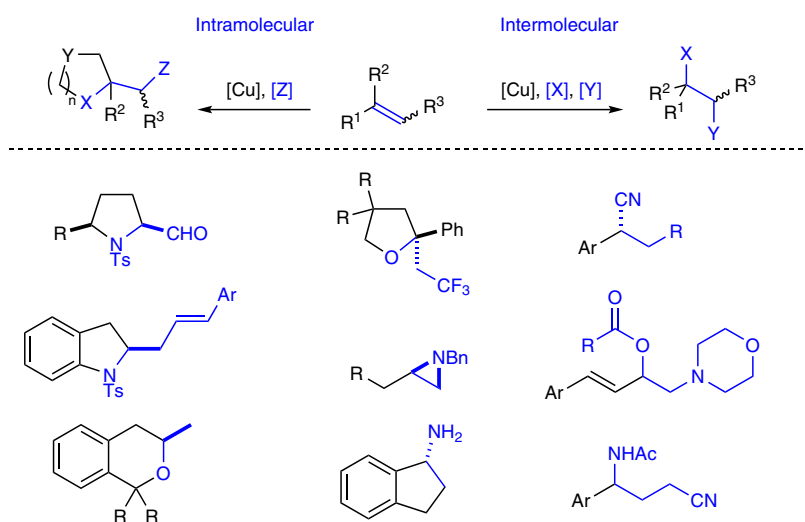


**Keywords:** copper(I) hydride · copper catalysis · alkenes · alkynes · aldehydes · ketones · hydroamination · hydrocarbonation · allylation · hydroboration

### 1.3 Copper-Catalyzed Alkene Difunctionalization

S. R. Chemler<sup>1b</sup> and J. J. Kennedy-Ellis<sup>1b</sup>

Alkene difunctionalization is a classic molecular transformation in organic synthesis, enabling the production of more-complex molecules from simple hydrocarbon-derived feedstocks. Alkene difunctionalizations catalyzed by copper complexes offer potentially more-sustainable protocols compared to those catalyzed by more-precious or -toxic metals. This chapter summarizes important recent advancements in the field, especially in the area of asymmetric catalysis. A number of copper-catalyzed intramolecular and intermolecular alkene difunctionalizations for the synthesis of cyclic and acyclic chiral amines and ethers, and related compounds, are presented. The reactions include alkene and/or diene hydroamination, hydroetherification, carboamination, carboetherification, diamination, oxyamination, and dicarbofunctionalization. Many of the reaction mechanisms involve a radical component either in the first or second bond-forming event. The ability of copper to engage with radicals in bond-forming events, including enantioselective ones, is a valuable aspect of many of these reactions.

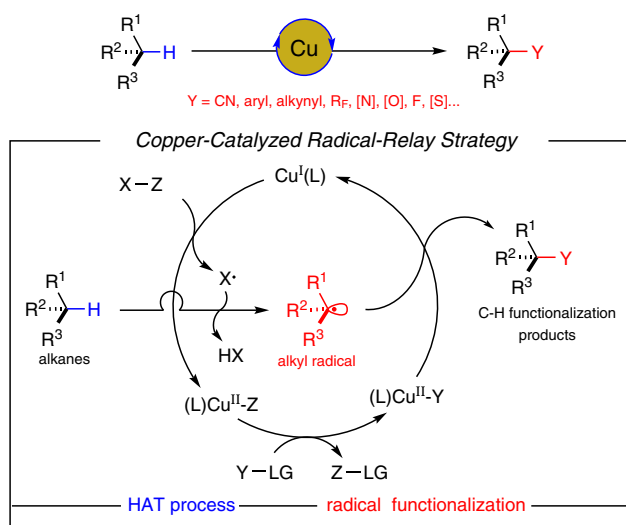


**Keywords:** alkenes · amines · amino alcohols · aminoxygenation · aziridines · carboamination · carboetherification · copper catalysis · diamination · dicarbofunctionalization · dienes · difunctionalization · enantioselective · ethers · hydroamination · hydroetherification · indolines · lactams · lactones · pyrrolidines · radicals

### 1.4 Copper-Catalyzed C–H Functionalization via Radicals

P. Chen<sup>1b</sup> and G. Liu<sup>1b</sup>

The direct functionalization of C–H bonds is highly attractive due to its efficiency for converting simple molecules into a wide range of valuable organic compounds. Among available strategies, radical C–H functionalization via hydrogen-atom transfer (HAT) represents one of the most powerful approaches and allows a unique profile of reactivity and selectivity. In this review, copper-catalyzed C–H functionalizations via radicals are summarized, including C–H cyanation, arylation, alkynylation, fluoroalkylation, amination, and oxygenation. It is worth noting that the combination of chiral ligands and chiral phosphoric acids with copper catalysis enables the enantioselective functionalization of radicals.

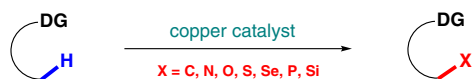


**Keywords:** copper catalysis · C–H bonds · C–H functionalization · radicals · cyanation · arylation · alkynylation · fluoroalkylation · amination · oxygenation · fluorination · thiolation · selanylation

### 1.5 Copper-Catalyzed Directed C–H Functionalization

H. Xu and H.-X. Dai<sup>1b</sup>

Copper-catalyzed C–H bond functionalization has attracted significant attention in recent years, and in this review the key achievements are summarized. Using this methodology, a variety of C–C and C–heteroatom bonds (including C–N, C–O, C–S, C–Se, C–halide, C–P, and C–Si) can be formed with the assistance of monodentate and bidentate directing groups.

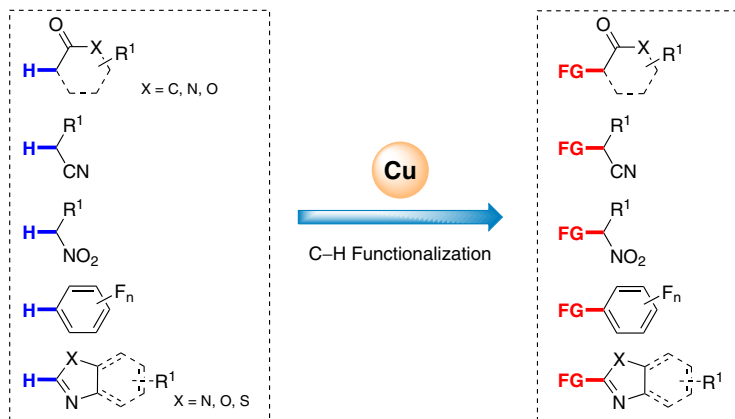


**Keywords:** base-metal catalysis • copper catalysis • directing groups • C–H functionalization • C–C bond formation • C–heteroatom bond formation

### 1.6 Copper-Catalyzed Acidic C–H Functionalization

Y. Shang<sup>1b</sup>, Y. Ren<sup>1b</sup>, and W. Su<sup>1b</sup>

Copper-catalyzed functionalization of acidic C–H bonds has emerged as a fruitful field due to the abundance and inexpensive nature of copper salts. In this chapter, we summarize the relevant advances in which copper promotes direct C–H functionalizations, including cross-dehydrogenative transformations, of activated organic substrates. The chapter is classified based on the types of activating group, including carbonyl, nitrile, nitro, as well as electron-deficient (hetero)aromatic groups.

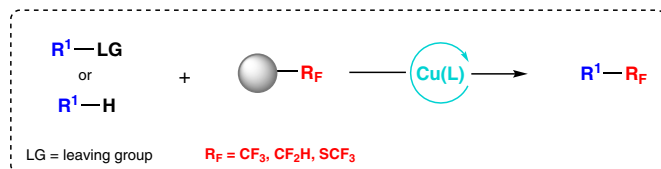


**Keywords:** copper catalysis • acidic C–H functionalization • carbonyl compounds • nitriles • nitroalkanes • polyfluoroarenes • heteroarenes • cross-dehydrogenative coupling

### 1.7 Copper-Catalyzed/Mediated Trifluoromethylation and other Fluoroalkylations

Y. Ouyang<sup>1b</sup>, J.-Y. Shou, and F.-L. Qing<sup>1b</sup>

The trifluoromethyl group and other fluoroalkyl groups have received great attention in organic and medicinal chemistry due to their unique properties, such as their strong electronegativity and high lipophilicity. Consequently, the development of methods for the introduction of trifluoromethyl and fluoroalkyl groups into organic molecules has recently seen remarkable progress. In this chapter, copper-catalyzed/mediated fluoroalkylation reactions, including trifluoromethylation, difluoromethylation, and trifluoromethylthiolation are summarized.

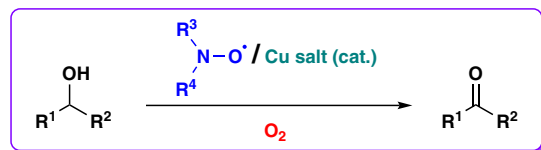


**Keywords:** copper-catalysis · trifluoromethylation · difluoromethylation · trifluoromethylthiolation · fluoroalkylation

### 1.8 Copper-Catalyzed Aerobic Oxidation of Alcohols


Y. Sasano<sup>1b</sup> and Y. Iwabuchi<sup>1b</sup>

The oxidation of alcohols to carbonyl compounds is one of the most important reactions in organic synthesis. Owing to current environmental concerns, catalytic alcohol oxidation using molecular oxygen as the terminal oxidant has been actively investigated. Copper is frequently used as an aerobic oxidation catalyst in organic syntheses, as well as in biological systems. Co-catalysts acting in coordination with copper to promote the aerobic oxidation of alcohols have been extensively investigated, and in this context the use of nitroxyl radicals has been identified as a promising strategy. Through the efforts of many researchers, nitroxyl radical/copper catalyst systems that efficiently oxidize traditionally more challenging aliphatic alcohols under mild conditions have recently been discovered. Methods for the synthesis of esters, imines, nitriles, amides, and imides by nitroxyl radical/copper-catalyzed aerobic alcohol oxidation in the presence of other alcohols, amines, and amides have also been developed. Nitroxyl radical/copper-catalyzed aerobic alcohol oxidation exhibits outstanding chemoselectivity, and efficiently converts alcohols bearing oxidation-prone functional groups that cannot be efficiently oxidized using conventional methods.

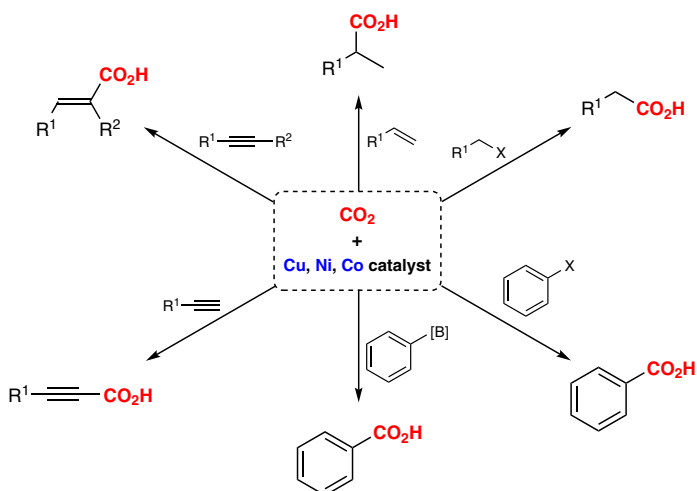


**Keywords:** copper catalysis · alcohols · aerobic oxidation · nitroxyl radicals · nitroxides · cooperative catalysis · chemoselectivity · aldehydes · ketones · lactones · esters · imines · nitriles · amides · imides · amino alcohols · sulfides · dithianes

### 1.9 Base-Metal-Catalyzed Carboxylation Using Carbon Dioxide

T. Fujihara 

Carbon dioxide (CO<sub>2</sub>) is the final product of hydrocarbon oxidation and is thermodynamically and kinetically stable. Therefore, efforts to find methods to activate and reuse this material under mild reaction conditions are required. To achieve efficient conversion, one solution is the use of transition-metal catalysts. This chapter reviews the process of catalytic carboxylation with carbon dioxide via carbon–carbon bond formation involving base-metal complexes (copper, nickel, and cobalt) as catalysts. These reactions are organized based on the metal used, and the reactions using each metal are classified according to substrate and reaction pattern.

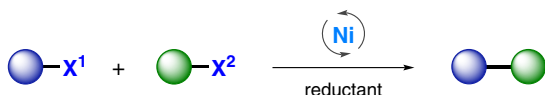


**Keywords:** carbon dioxide · carboxylation · carboxylic acids · copper · nickel · cobalt · alkynes · alkenes · dienes · organoboranes · aryl halides · alkyl halides · transition-metal catalysis

### 1.10 Nickel-Catalyzed Cross-Electrophile Coupling Reactions

X.-Z. Shu  and X. Pang

Nickel-catalyzed cross-electrophile coupling has become a powerful tool for the construction of molecules. These new bond-forming reactions bypass the requirement for the handling of organometallic reagents and are selectively orthogonal to classic cross couplings. This chapter provides a brief review of the achievements in this field. Selected methods for C–C coupling with a variety of reacting partners are presented. In addition to transformations involving a metal reductant, representative examples of nickel metallaphotocatalysis and electrochemical nickel catalysis are also discussed. Finally, expansion of this chemistry to the reactions of heavier group 14 electrophiles is described.

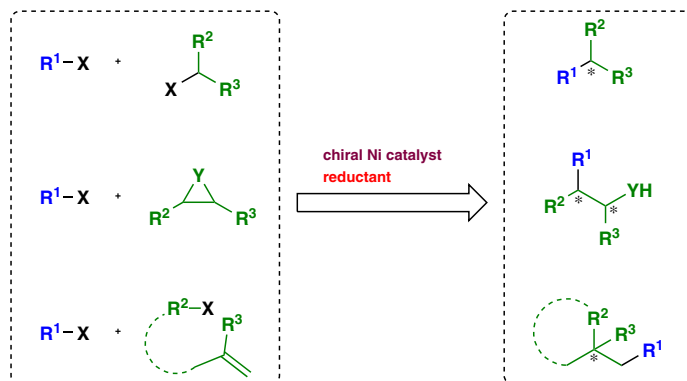


**Keywords:** nickel catalysis · cross coupling · reductive coupling · cross-electrophile coupling · alkylation · arylation · alkenylation · silylation · germylation · photocatalysis · electrocatalysis · silicon · germanes · stannanes

### 1.11 Nickel-Catalyzed Enantioselective Reductive Cross-Coupling Reactions


C. Wang  and F. Yang

Nickel-catalyzed enantioselective reductive cross-coupling reactions enable simple and efficient synthesis of enantioenriched compounds, with high functionality tolerance, through circumventing the use of pregenerated organometallics. In this chapter, the most quintessential examples of the recent advances in this field have been summarized, and the contents are organized according to the reaction types.

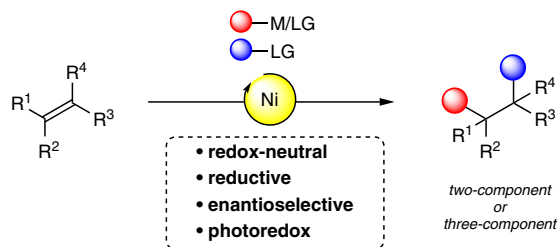


**Keywords:** nickel catalysis · reductive cross coupling · cross-electrophile coupling · asymmetric catalysis · ring-opening reactions · dicarbofunctionalization · Heck reaction · arylation · alkylation · carbamoylation · acylation · vinylation · organohalides · epoxides · aziridines · cyclobutanones · alkenes · oxindoles · indanes · indanones

### 1.12 Nickel-Catalyzed Alkene Dicarbofunctionalization

B. C. Lee, L. Lin, C. Ko, and M. J. Koh 

The transition-metal-catalyzed cross-coupling reactions of alkenyl compounds remain one of the most versatile ways of forming C—C bonds from organohalide and organometallic species. The application of inexpensive, readily available, and non-toxic base metals, such as nickel, as catalysts gives rise to a powerful approach to access highly substituted molecules via dicarbofunctionalization. A wide array of nucleophiles and/or electrophiles can be employed, and various mechanisms have been proposed. Generally, these mechanisms can be classified as redox-neutral, reductive, asymmetric, and photoredox dicarbofunctionalizations. In this chapter, we will highlight the recent advances made in the field of nickel-catalyzed alkene dicarbofunctionalization.

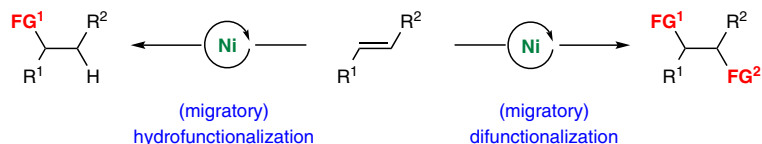


**Keywords:** nickel catalysis · dicarbofunctionalization · alkenes · metallaphotoredox · photoredox catalysis · asymmetric catalysis · reductive coupling · two-component dicarbofunctionalization · three-component dicarbofunctionalization

## 1.13 Nickel-Catalyzed Cross Coupling Involving Alkenes

S. Zhu<sup>1b</sup>

Nickel-catalyzed functionalization of alkenes to give value-added products in a manner that is rapid, selective, and modular has resulted in tremendous advances in synthetic chemistry. Great progress has been achieved in nickel-catalyzed (migratory) hydrofunctionalization and difunctionalization of alkenes over the past few years. In the first half of this chapter, nickel-catalyzed (migratory) hydrofunctionalization of alkenes is described. The second half details nickel-catalyzed difunctionalization of alkenes. Both reductive and redox-neutral reactions are discussed.



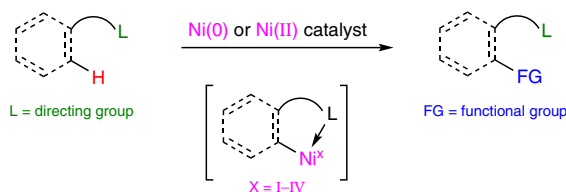
FG = functional group

**Keywords:** alkenes · asymmetric catalysis · chain-walking · cross-coupling reactions · difunctionalization · hydrofunctionalization · isomerization · metal hydrides · nickel catalysis · regioselectivity · transition-metal catalysis

## 1.14 Nickel-Catalyzed Directed C–H Functionalization

N. Chatani<sup>1b</sup>

This chapter summarizes some selected examples of nickel-catalyzed directed C–H functionalization reactions that involve the activation of a C–H bond as a key step. It is now recognized that nickel complexes, mostly nickel(0) and nickel(II), are some of the most attractive and effective catalysts for the development of C–H functionalization reactions because of the low cost and earth-abundance of nickel, and, most importantly, because the complexes can exist in various oxidation states (+1, +2, +3, and +4) during the transformation, which leads to unique reactivity.

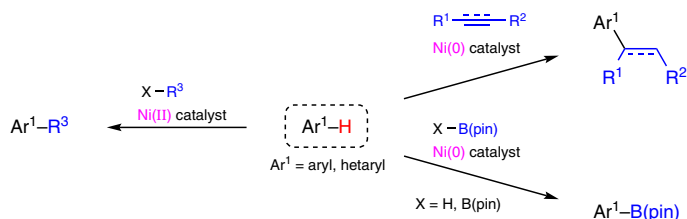


**Keywords:** nickel catalysis · C–H activation · C–H alkylation · C–H alkynylation · C–H amination · C–H annulation · C–H arylation · C–H functionalization · directing groups

## 1.15 Nickel-Catalyzed Nondirected C–H Functionalization

Y. Nakao<sup>1b</sup>

This chapter summarizes some selected examples of nickel-catalyzed nondirected C–H functionalization reactions. Nickel(0) complexes have been demonstrated to be effective for C–H alkylation and alkenylation reactions of arenes and heteroarenes through a ligand-to-ligand hydrogen-transfer mechanism for C–H activation that is unique to nickel-catalyzed approaches. They also effect the C–H borylation of arenes and heteroarenes. Some nickel(II) complexes are shown to catalyze cross-coupling-type transformations of heteroarenes with organic electrophiles through C–H activation by nickel(II) intermediates.

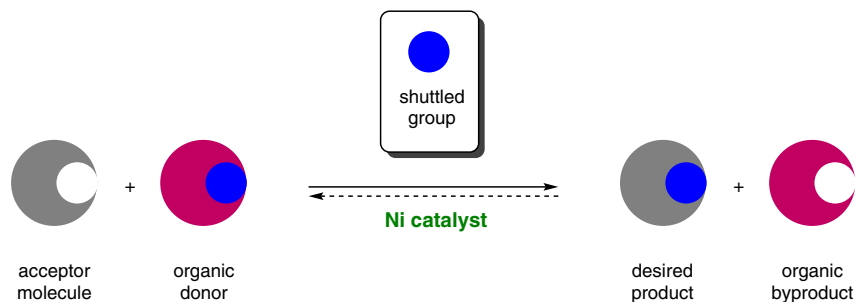


**Keywords:** base-metal catalysis · C–H activation · C–H alkylation · C–H alkenylation · C–H arylation · C–H alkynylation · C–H borylation · C–H functionalization · nickel catalysis

## 1.16 Nickel-Catalyzed Bond Activation for Functional-Group Shuttling

T. Delcaillau and B. Morandi<sup>1b</sup>

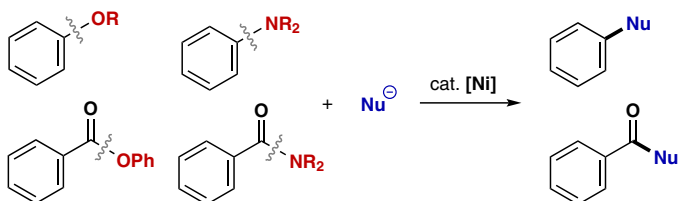
Functional-group shuttling, for example through shuttle catalysis or single-bond metathesis, has recently emerged as a powerful tool in targeted organic synthesis. This concept offers several advantages in comparison with traditional catalytic reactions. It enables the use of more-benign surrogates as formal functional-group donors, leading to safer reaction profiles. These reactions also often complement traditional cross-coupling reactions by allowing for base-free conditions, since no external inorganic reagent is required. Lately, nickel has emerged as an extremely useful transition metal in catalysis, complementing and often even surpassing the efficiency of noble metals, such as palladium. The focus of this chapter is to summarize recent developments in nickel-catalyzed functional-group-shuttling reactions.



**Keywords:** nickel catalysis · functional-group shuttling · shuttle reactions · carbocyanation · hydrocyanation · cyanation · cross coupling · carboxylation · sulfanylation

**1.17 Nickel-Catalyzed Cross-Coupling via C–O and C–N Activation***T. Yoshida and M. Tobisu* 

The use of a suitable nickel catalyst enables inert phenol derivatives (i.e., aryl ethers and esters) and aniline derivatives to be used as aryl halide surrogates in cross-coupling reactions, via the activation of C–O and C–N bonds. In this review, standard procedures for such reactions are presented.



**Keywords:** nickel catalysis · cross-coupling reactions · C–O activation · C–N activation · phenols · anilines · arylation · alkylation · alkynylation · amination · silylation · borylation · reduction · cyclization · heterocycles