Catalysis Science & Technology

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

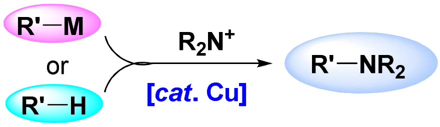
www.rsc.org/catalysis

Recent Progress in Copper-Catalyzed Electrophilic Amination

Xiaoyu Yan[a], Xianghua Yang[b], Chanjuan Xi[a]*

[a]Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, China

[b]School of Chemical Engneering & Light Industry, Guangdong University of Technology, Guangzhou 510006, Guangdong, China



This perspective encompasses the recent trends and developments in copper-catalyzed electrophilic amination for construction of various amines and their derivatives.

Recent Progress in Copper-Catalyzed Electrophilic Amination

Xiaoyu Yan[a], Xianghua Yang[b], Chanjuan Xi[a]*

[a]Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, China

[b]School of Chemical Engneering & Light Industry, Guangdong University of Technology, Guangzhou 510006, Guangdong, China

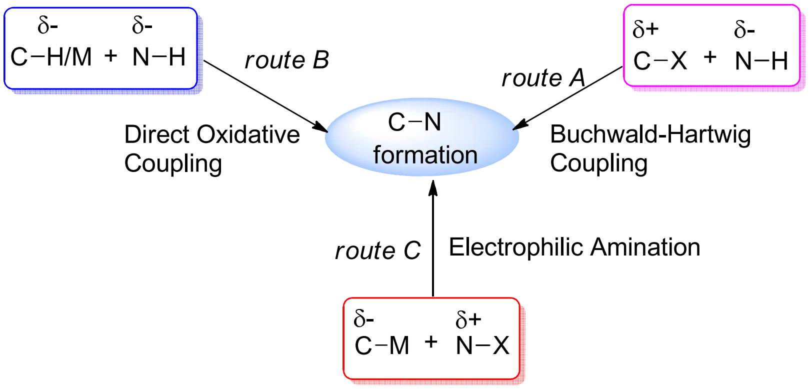
cjxi@tsinghua.edu.cn

Abstract: Copper-catalyzed coupling reactions have been recognized as one of the most useful strategies for the formation of C-N bond. This perspective gives an overview of recent developments in copper-catalyzed electrophilic amination for construction of various amines and their derivatives, including electrophilic amination of various organometallic reagents and direct C-H bond as well as annulative electrophilic amination of *o*-alkynylphenols and *o*-alkynylanilines.

1. Introduction

Amines are privileged structural motifs in many biologically active compounds, pharmaceutical targets, and functional materials.[1] Metal-promoted C-N cross-coupling reactions provide a powerful and convergent approach to amines and their derivatives. Recently, Pd- or Cu-catalyzed process from nucleophilic amines with electrophilic aryl halides (Buchwald-Hartwig C-N coupling reaction) is extensively explored in this field (Scheme 1, route A).[2] It is now the most powerful and reliable method for the synthesis of amines and their derivatives. Recent advances in metal-mediated C-H functionalization chemistry have enabled the direct oxidative

C-H/N-H coupling to be a complementary and potentially more effective process for the synthesis of the amines (Scheme 1, route B).[3] In addition, Cu-mediated oxidative amination of nucleophilic arylboronic acids with amines (Chan-Lam-type coupling) is a hallmark reaction in this filed.[4] On the other hand, an umpolung strategy - electrophilic amination using a reagent of type R_2N^+ was considered as a viable alternative for the formation of C-N bond and will remain an active area in constructing amines and their derivatives (Scheme 1, route C).

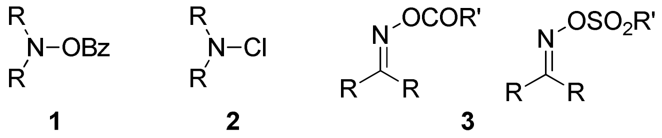


Scheme 1 Construction of C-N bond via cross-coupling reactions

To date there are many reports on the formation of C-N bond via electrophilic amination of carbanions and enolates with aminating reagents.[5] Most of these reactions need active organometallic reagents such as RMgX or RLi, which are less substrate-tolerant. Due to the oxidizability of electrophilic nitrogen sources, direct reactions of organometallic reagents with aminating reagents often afford the products in modest yield. In general, Pd, Rh, Ru, Ir, Ni, Cu, and Fe complexes are the most investigated catalysts for these coupling reactions. Although different advantages could be specifically ascribed to each of these metals, Cu-catalysis represents a promising direction in C-N formation reaction, due to its low cost, low toxicity, easy handle, and high efficiency. In this perspective, we focused on recent advances in the field of copper-catalyzed electrophilic amination.

2. Electrophilic Aminating Reagents

In an electrophilic amination reaction, amino or substituted amino groups were transferred from certain aminating reagents to nucleophiles. Such reagents usually contain an electron-withdrawing functional group attached to nitrogen which would induce a partial positive charge at the nitrogen atom. Up to now, various types of aminating reagents such as *N*-haloamines, substituted hydroxylamines, oxaziridines, oximes, diazonium salts, azodicarboxylates, and azides were reported to be effective. Three kinds of electrophilic aminating reagents, *O*-benzoylhydroxylamines **1**, *N*-chloroamines **2** and oxime esters **3** were most frequently used in recent copper-catalyzed electrophilic amination reactions and were discussed herein.

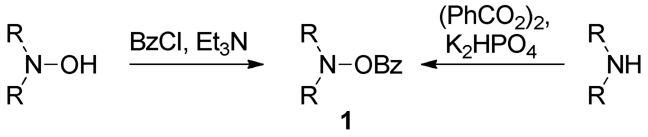


Scheme 2 Typical electrophilic aminating reagents: *O*-benzoylhydroxylamines **1**, *N*-chloroamines **2**, and oxime esters **3**

2.1 *O*-Benzoylhydroxylamines

O-benzoylhydroxylamines are the most widely used electrophilic aminating reagents amongst a number of *O*-substituted hydroxylamines. They can be easily prepared, either by benzoylation of hydroxylamines in the presence of a base (Scheme 3, left side)[6] or *via* oxidation of secondary amines with benzoyl peroxide and an exogenous inorganic base in ethereal solvent as reported by Ganem and coworkers

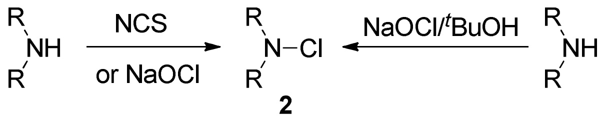
(Scheme 3, right side).[7] Furthermore, Johnson and coworkers discovered that oxidation of primary and secondary amines with benzoyl peroxide would afford *O*-benzoylhydroxylamines with high yields in a polar aprotic solvent at room temperature.[6]



Scheme 3 Synthesis of *O*-benzoylhydroxylamines

2.2 *N*-Chloroamines

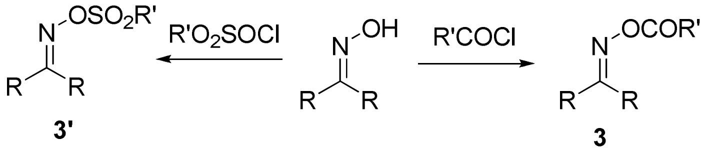
N-Chloroamine was one of the earliest investigated reagents for electrophilic amination. It can be prepared by treating the corresponding amines with NCS (*N*-chlorosuccinimide) or NaOCl (Scheme 4, left).[8] Zhong reported a modified protocol for the preparation of *N*-chloroamines via *in situ* generation of *tert*-butyl hypochlorite by NaOCl and ^{t}BuOH (Scheme 4, right).[9] In these procedures, the *N*-chloroamines can all be isolated simply by extraction.



Scheme 4 Synthesis of *N*-chloroamines

2.3 Oxime esters

Oxime esters such as *O*-acyloximes and *O*-sulfonyloximes are a class of aminating reagents which were widely used in the electrophilic amination. The *O*-acyloximes and *O*-sulfonyloximes can be prepared by direct benzoylation or sulfonylation of oximes (Scheme 5),[7] which were obtained quantitatively via reaction of ketones or aldehydes with hydroxylamine hydrochloride.



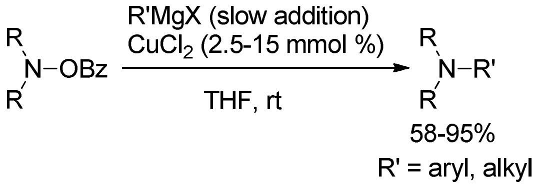
Scheme 5 Synthesis of oxime esters

3. Electrophilic amination with various nucleophilic organometallic reagents

The electrophilic amination of carbanions, i.e., the conversion of organometallic compounds to amines has been known for a long time, and a large number of organometallic compounds were successfully employed in electrophilic amination under catalyst-free or catalytic condition. In this perspective, only the copper-catalyzed ones were listed.

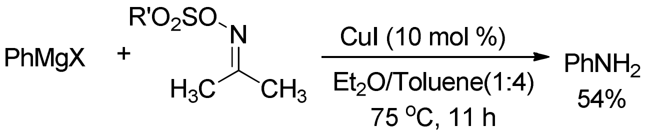
3.1 Electrophilic amination with Grignard reagents

Grignard reagents (RMgX) can react with parent haloamine or alkylhydroxylamine to yield primary amines. This method was broadly applied on the attachment of amino group to organometallic compounds.[5e] However, for reactions with *N*-substituted haloamine and hydroxylamine, the yields of the corresponding amines were rather low due to occurrence of side reactions such as halogenation and elimination. Johnson and coworkers reported a $CuCl_2$-catalyzed amination reaction of Grignard reagents with *O*-acylhydroxylamines (Scheme 6).[11] Both aryl and alkyl Grignard reagents were converted into the corresponding amines in good to high yields. In this amination process, the side reaction (C-acylation) was greatly decreased in the presence of catalytic amount of $CuCl_2$.



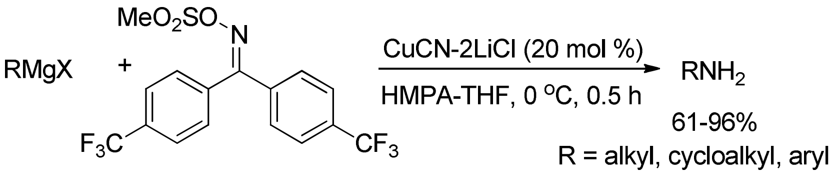
Scheme 6 $CuCl_2$-catalyzed amination of Grignard reagents

Reaction of phenylmagnesium bromide with *O*-(2,4,6-trimethylphenylsulfonyl)-oxime in a mixed solution of diethyl ether-toluene (1:4 by volume) at 75 ºC would give aniline with 58% yield after 40 h. When the reaction was treated with 10 mol % of CuI, the reaction time decreased to 11 h without a significant change in the yield (Scheme 7).[12]



Scheme 7 CuI-catalyzed amination of Grignard reagents

Narasaka and coworkers used benzophenone *O*-sulfonyloxime derivatives for the electrophilic amination of alkyl-, cycloalkyl-, and arylmagnesium reagents. 4,4'-Bis(trifluoromethyl)benzophenone *O*-methylsulfonyloxime was reacted with primary-, secondary-, tertiary-, and cycloalkylmagnesium reagents in THF-HMPA solution at 0 ºC in the presence of CuCN·2LiCl as catalysts, furnishing the corresponding amines in high yields (Scheme 8).

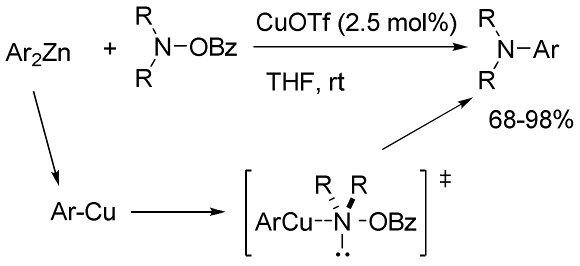


Scheme 8 CuCN·2LiCl-catalyzed amination of Grignard reagents

3.2 Electrophilic amination with organozinc reagents

Organozinc compound is an important class of main-group organometallic reagents. The bonds between carbon and zinc have some covalent features, therefore, they display modest reactivities towards many electrophilic reagents. Such characteristics allow them to tolerate numerous functional groups:[14] a number of electrophilic amination procedures have been reported in literature directly employing organozinc reagents.[15]

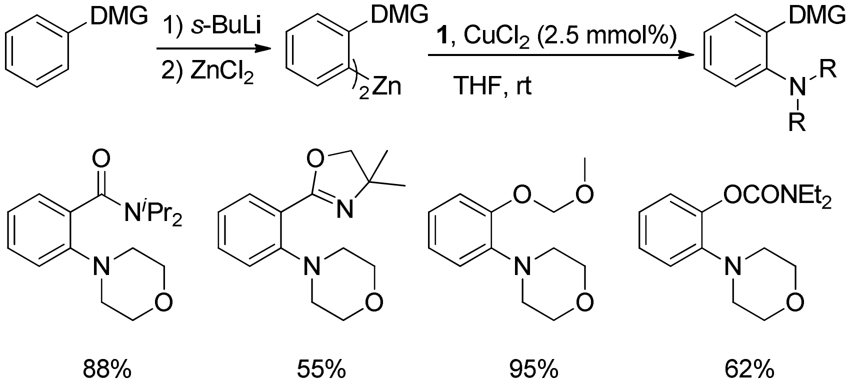
In 2004, Johnson and coworkers reported their pioneering work on copper-catalyzed electrophilic amination of diorganozinc reagents.[16] *O*-Benzoylhydroxylamines were employed in this reaction, affording tertiary amines with hindered substituents in high yields catalyzed by CuOTf (Scheme 9). It is noteworthy that it is convenient both in terms of reaction conditions (room temperature, ≤1 h) and ease of product isolation (acid/base extractive workup). This reaction also exhibited great functional group tolerance such as CN, CO_2R, NO_2, OTf, X etc.[17] The mechanism of the process was also investigated and subsequent transmetalation and S_N2 reaction on nitrogen atom were suggested.[11]



Scheme 9 CuOTf-catalyzed amination of diorganozinc reagents

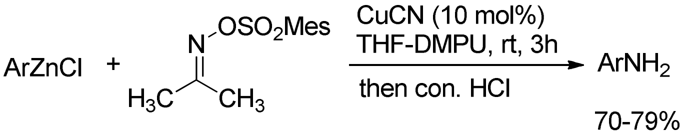
Caution: Copper-catalyzed amination of diorganozincs is an exothermic reaction. The released heat hardly affects the reaction yield on a micro-scale. However, when the reaction is performed on a large-scale, the yield would decrease significantly if the reaction temperature is not kept at 5 ºC.[18]

Directed *ortho* lithiation was a reliable tool for the functionalization of poorly reactive C$_{aryl}$-H bonds. Combined with directed *ortho* metalation / transmetalation / catalytic amination, the *ortho*-amination of C-H reaction was achieved in one-pot, affording the functionalized anilines in high yields (Scheme 10).[6]



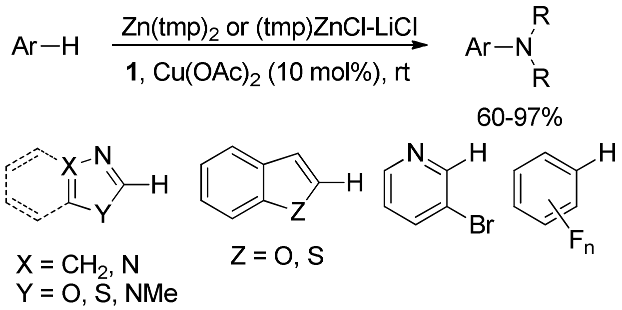
Scheme 10 Directed *ortho* metalation/amination reactions

CuCN-catalyzed amination of organozinc chlorides and diorganozincs with *O*-sulfonyloxime at room temperature gives primary amines at low to moderate yields. Addition of a dipolar aprotic solvent as co-solvent leads to increased yields (Scheme 11),[19] while addition of a P-, N-, or S-donor ligand would significantly decrease the quantity of copper catalysts as well as a remarkable increase in the yield.[20]



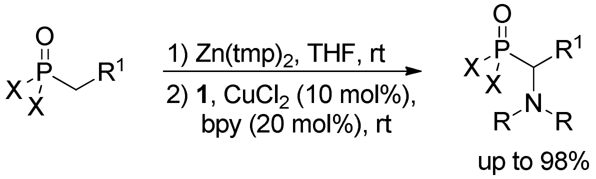
Scheme 11 CuCN-catalyzed amination of organozinc reagents

Recently, Wang's group reported a direct amination of heteroarenes and arenes through a one-pot C-H zincation and copper-catalyzed electrophilic amination procedure. This procedure provided an efficient and rapid approach to access a diverse range of heteroaromatic and aromatic amines (Scheme 12). Its mild reaction conditions and good functional-group compatibility demonstrated the potential for synthesis of important and complex amines.[21]



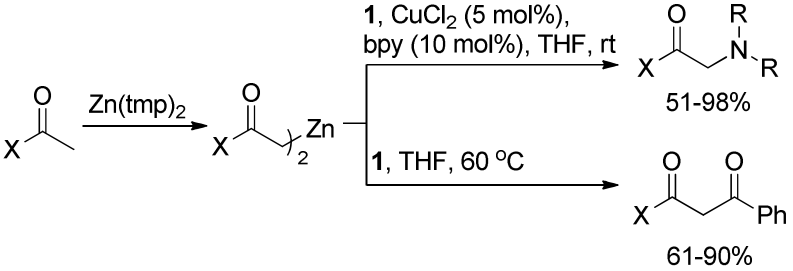
Scheme 12 $Cu(OAc)_2$-catalyzed amination of heteroarenes and arenes

This C-H zincation / electrophilic amination protocol can also be applied to acidic *sp*^{3} C-H bond. Wang and coworkers also reported a zincation/electrophilic amination approach to α-amino phosphonic acids and their derivatives (Scheme 13). This α-amination strategy enables the direct introduction of a variety of acyclic and cyclic amines to the *α*-position of phosphonates and phosphine oxides for the first time.[22]



Scheme 13 $CuCl_2$-catalyzed amination of phosphonates and phosphine oxides

Under similar conditions, α-amination reactions of esters and amides were achieved via a copper-catalyzed electrophilic amination of their zinc enolates using *O*-acylhydroxylamines. It is worth mentioning that, in the absence of a copper catalyst, the direct treatment of zinc enolates with *O*-acylhydroxylamines would form α-acylated 1,3-dicarbonyl products exclusively (Scheme 14).[23] This also provide an insight into the dual electrophilic reactivity of *O*-acylhydroxylamines for selective amination and acylation reactions of other C–H bonds.

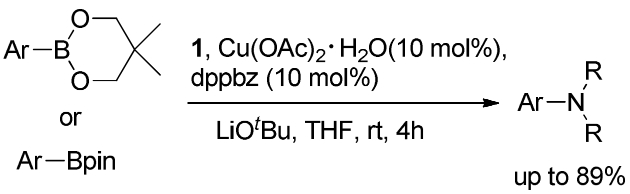


Scheme 14 Selective α-amination and α-acylation of esters and amides

3.3 Electrophilic amination with organoboronic acids

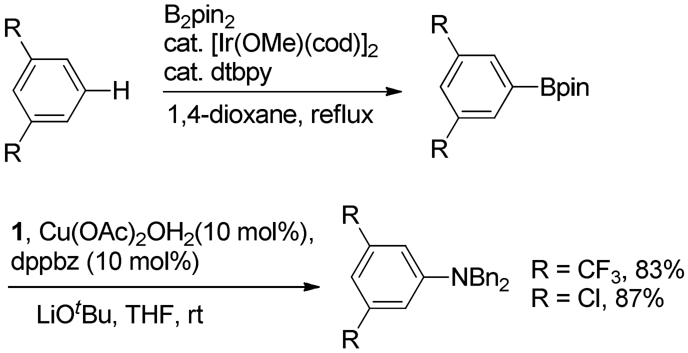
Organoboronic acids and their derivatives are used extensively in organic chemistry as building blocks or intermediates predominantly in the cross-coupling reactions.[24] They are generally stable, readily available, and compatible with a wide range of functional groups. In 1998, the groups of Chan， Lam, and Evans independently developed Cu-mediated oxidative coupling reactions between nucleophilic arylboronic acids / esters and amines.[4] This reaction, named Chan-Lam coupling, provided a complementary method for the formation of aniline derivatives. However, this method can only be applied to a limited scope of amine substrates.

In 2012, Miura and coworkers reported a $Cu(OAc)_2 \cdot H_2O$-catalyzed electrophilic amination of arylboronates with *O*-benzoylhydroxylamines (Scheme 15).[25] This umpolung amination approach enables the use of secondary acyclic amines, which are substrates with relatively low reactivity for conventional Chan-Lam coupling. Moreover, the catalysis accommodates a diverse set of functional groups including chlorides, bromides and iodides, as well as aldehydes, ketones, and esters.



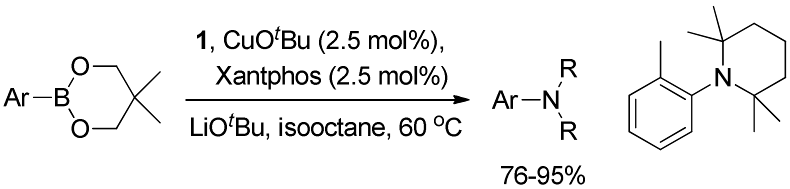
Scheme 15 $Cu(OAc)_2$-catalyzed amination of arylboronates

Moreover, the $Cu(OAc)_2{\cdot}H_2O$-catalyzed electrophilic amination of arylboronates can be easily combined with the iridium-catalyzed direct C-H borylation[26] of simple arenes. For example, 1,3-disubstituted benzenes were converted to the corresponding anilines in one-pot as shown in scheme 16.



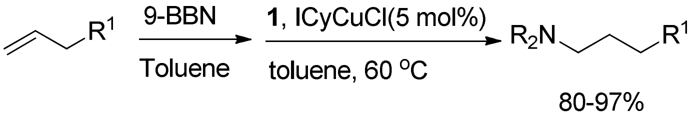
Scheme 16 C-H borylation/electrophilic amination sequence

Lalic's group also reported a CuO^tBu-catalyzed electrophilic amination reaction for the synthesis of hindered anilines from aryl and heteroaryl boronic esters, which is compatible with a wide variety of functional groups (Scheme 17).[27]



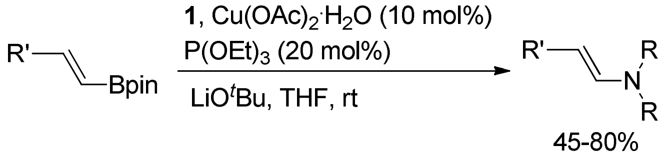
Scheme 17 CuO^tBu-catalyzed amination of arylboronates

Later on, Lalic and coworkers reported a ICyCuCl-catalyzed amination of alkyl boranes through hydroboration of alkenes.[28] This one-pot procedure involves the hydroboration of an alkene followed by a novel electrophilic amination of the alkyl borane catalyzed by an NHC-Cu complex. Terminal alkenes are successfully transformed into tertiary alkyl amines bearing a variety of functional groups. It also provides a novel procedure for *anti*-Markovnikov hydroamination of alkenes (Scheme 18).



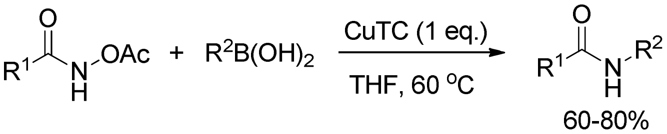
Scheme 18 Hydroamination of alkenes

The amination of alkenylboranes was also achieved in a $Cu(OAc)_2 \cdot H_2O/P(OEt)_3$ catalyzed system (Scheme 19).[29] Furthermore, sequential Zr/Cu catalysis for formal anti-Markovnikov hydroamination of terminal alkynes afforded enamines in one-pot.



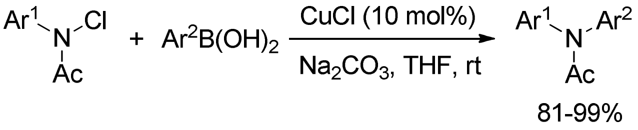
Scheme 19 $Cu(OAc)_2$-catalyzed amination of alkenylboronates

The electrophilic amidation of aryl, heteroaryl, and alkenyl boronic acid with *O*-acetyl hydroxamic acids was reported by Liebeskind's group (Scheme 20).[30] A stoitiometric amount of CuTC was required for this procedure. Nonetheless, it allows the easy preparation of a variety of amides and is a useful complement to existing metal-catalyzed methods for C-N bond formation.



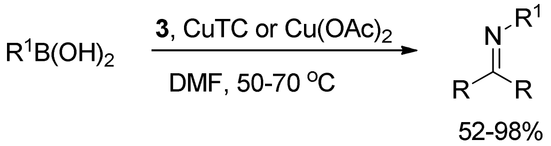
Scheme 20 CuTC-mediated electrophilic amidation of boronic acid

Utilizing an easily prepared and highly reactive *N*-chloroamide compound, Lei and coworkers developed an efficient copper-catalyzed electrophilic amination of arylboronic acids.[31] The transformation yielded high in the formation of diarylamides and tolerated a wide variety of functional groups, including iodo, bromo, and chloro moieties, which are typically sensitive in palladium-catalyzed reactions (Scheme 21).



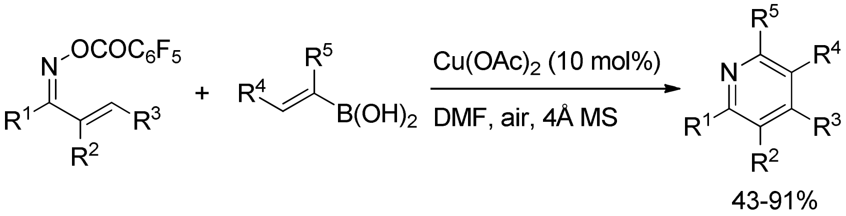
Scheme 21 CuCl-catalyzed electrophilic amidation of boronic acid

An copper-catalyzed *N*-imination of boronic acids was also developed.[32] The reaction used *O*-acyl ketoximes as the iminating agent and proceeded under nonbasic and nonoxidizing conditions, thus complementing the existing C-N bond forming reactions (Scheme 22). This method tolerates various functional groups and takes place efficiently using aryl, heteroaryl, and alkenyl boronic acids.



Scheme 22 CuTC-catalyzed imination of boronic acids

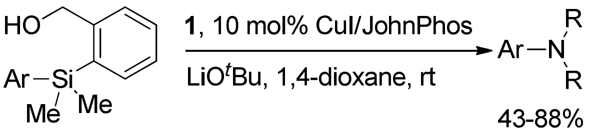
Liebeskind and coworkers further developed a simple and modular method to get highly substituted pyridines.[33] It's a cascade reaction comprising: (1) a novel *N*-iminative, Cu-catalyzed cross-coupling of alkenylboronic acids at the N-O bond of *α*,*β*-unsaturated ketoxime *O*-pentafluorobenzoates, (2) electrocyclization of the resulting 3-azatriene, and (3) air oxidation, affording highly substituted pyridines in moderate to excellent isolated yields (Scheme 23).



Scheme 23 Cu(OAc)$_2$-catalyzed synthsis of pyridines by imination/cyclization

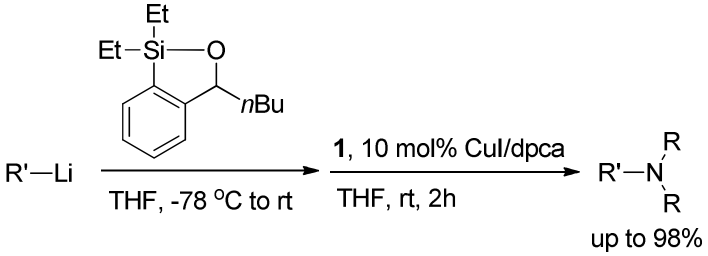
3.4 Electrophilic amination with organosilicon reagents

It was reported that the oxidative coupling reaction of organosilicon reagents with a variety of N-H containing substrates afforded amines and derivatives. However, either stoichiometric amounts of copper salts[34] or tetrabutylammonium fluoride (TBAF)[35] as additive was required. Miura and coworkers developed a copper-catalyzed electrophilic amination of aryl[(2-hydroxymethyl)phenyl]-dimethylsilanes with *O*-acylated hydroxylamines (Scheme 24).[36] This strategy allows arylsilanes to serve as an efficient aryl source for the construction of aniline derivatives. Moreover, the high halogen compatibility of the process provides a facile access to bromide-substituted arylamines and complements the conventional Pd-based amination chemistry.



Scheme 24 CuI-catalyzed amination of organosilicon reagents

Amos and co-workers developed a copper-catalyzed electrophilic amination of aryl and heteroaryl organolithiums with *O*-benzoylhydroxylamines, using recoverable siloxane as the transfer agent (Scheme 25).[37] It involves a reaction of organolithiums with siloxane and an electrophilic amination of the *in situ* prepared silanes. The use of siloxane transfer agents offers a viable solution for the direct application of organolithiums in electrophilic amination.

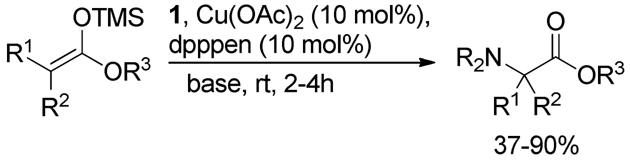


Scheme 25 Electrophilic amination of organolithiums employing siloxane transfer agent

3.5 Electrophilic amination with silyl ketene acetals

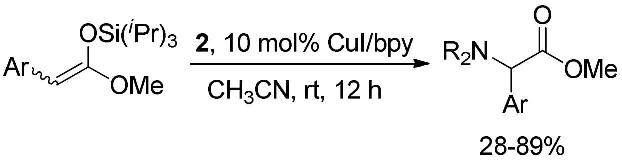
α-Amination of carbonyl compounds drew much attentions because α-Amino acids and their derivatives are fundamental and important structural motifs in many biologically active compounds and pharmaceutical targets, especially peptide drugs. A traditional α-halogenation of carbonyls and subsequent nucleophilic substitution with amines is practical, but often suffers from low efficiency and fiercing conditions. To overcome these limitations, electrophilic aminations of carbonyl compounds and derivatives with different amination reagents were explored.

Silyl ketene acetals are commonly used as nucleophilic reagents in aldol, Michael, and Mannich reactions. Miura et al developed a copper-catalyzed amination of ketene silyl acetals with *O*-benzoylhydroxylamines, directing to the synthesis of unnatural α-amino acids (Scheme 26).[38] It provides a brand new C-N bond-forming approach to α-amino acids starting from substrates at the carboxylic acid oxidation level.



Scheme 26 Cu(OAc)$_2$-catalyzed amination of silyl ketene acetals

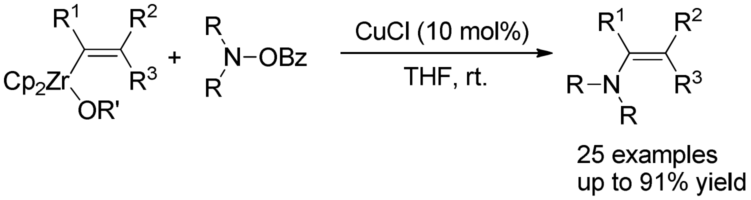
The amination of silyl ketene acetals with *N*-chloroamines was also investigated by Miura and coworkers.[39] Using CuI/bpy as the catalyst, α-amino acids were obtained with high yields under mild conditions (Scheme 27). The facile availability of *N*-chloroamines from secondary amines permits a one-pot two-step synthesis of α-amino acids starting from amines on a gram scale.



Scheme 27 CuI-catalyzed amination of silyl ketene acetals

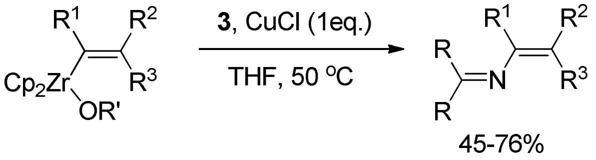
3.6 Electrophilic amination with organozirconium reagents

So far, most of electrophilic amination reactions were achieved with main-group organometallic reagents. Jarvo and coworkers reported a titanium-mediated amination of Grignard reagents with *N*-chloroamines, which was generated *in situ* from amines and NCS.[40] Aryltitanium, produced *in situ* by reacting of ArMgX with Ti(O^{i}Pr)$_4$, is a suitable nucleophilic reagent to react with *N*-chloroamines, forming amines in good yields. As part of an ongoing program in our laboratory to systematically study zirconocene chemistry, we reported a copper-catalyzed amination of alkenylzirconocenes with *O*-benzoylhydroxylamines, affording a wide range of enamines under mild conditions (Scheme 28).[41] The double bond was retained during the whole process. This reaction also tolerates a wide range of functional groups and can be used for preparation of hindered enamines. Mechanistically, we proposed that the alkenylzirconocene undergoes transmetalation with CuCl before amination.



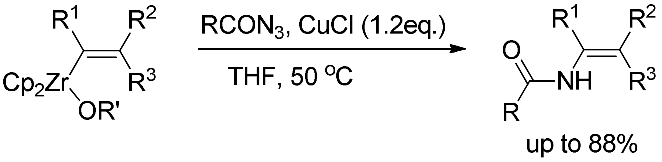
Scheme 28 CuCl-catalyzed amination of alkenylzirconocene

When *O*-benzoyloximes were utilized, electrophilic imination with alkenylzirconocenes would afford 2-azadienes in the present of a stoichiometric amount of CuCl (Scheme 29).[42] Both *O*-benzoylketoximes and *O*-benzoylaldoximes can be employed in this reaction. The configurations of the C=C and C=N double bonds persisted during the imination.



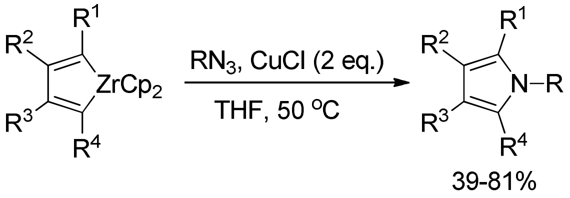
Scheme 29 CuCl-mediated imination of alkenylzirconocene

The amidation reaction of alkenylzirconocenes with acyl azides was also investigated (Scheme 30).[43] This reaction can be used to prepare various multi-substituted enamides.



Scheme 30 CuCl-mediated amidation of alkenylzirconocene

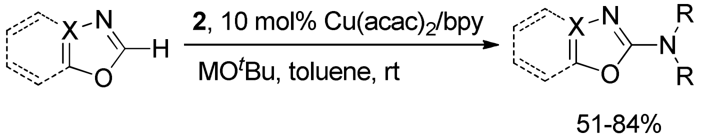
Zirconacyclopentadienes were considered as two alkenylzirconocenes. When they were treated with azides, pyrroles formed via double amination (Scheme 31).[44] It offers a new approach to multi-substituted pyrroles through Zr/Cu mediated cyclization of two alkynes and one azide in one-pot.



Scheme 31 Reaction of zirconacyclopentadienes with azides

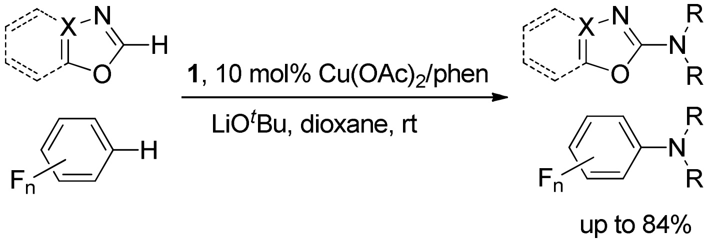
4. Electrophilic amination of direct C-H bond

Complementary to the electrophilic amination with organometallic reagents, direct C-H amination with electrophilic aminating reagents provides a new and potentially more effective C-N bond formation approach, although several effective metal-catalyzed C-H/N-H coupling methods were achieved via oxidative coupling.[3] The first direct C–H amination was reported by the group of Miura, which is a Cu-catalyzed reaction of N-chloroamines and azoles (Scheme 32).[45] This reaction proceeded under rather mild conditions and accessed straightforward to the heteroarylamines.



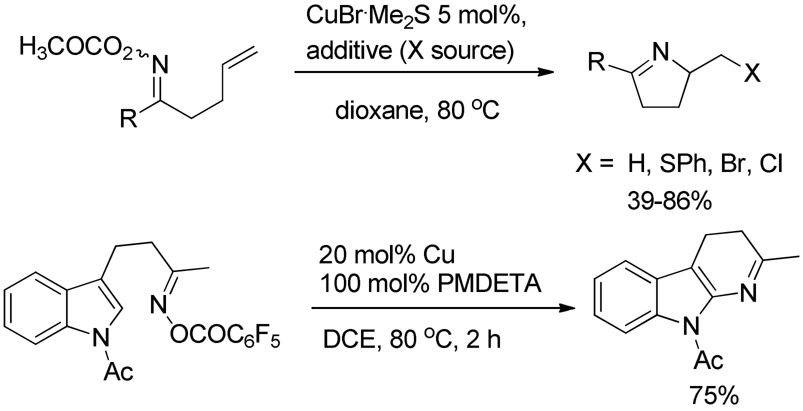
Scheme 32 Cu(acac)$_2$-catalyzed direct C–H amination of azoles

Miura's group also investigated the C–H amination of polyfluoroarenes and azoles with *O*-benzoylhydroxylamines (Scheme 33).[46] The catalysis enabled a rapid and concise construction of polyfluoroanilines and aminoazoles, which are vital in pharmaceutical and medicinal chemistry.



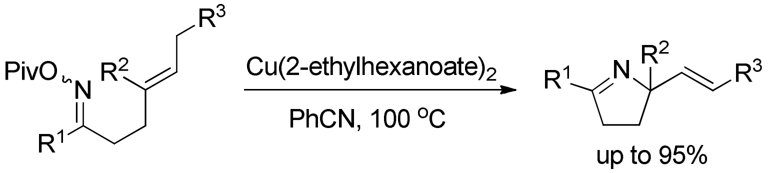
Scheme 33 Cu(OAc)$_2$-catalyzed direct C–H amination of azoles and polyfluoroarenes

As early as 2002, Narasaka and coworkers reported an intramolecular amination of oximes derivatives. The radical cyclization of *γ*, *δ*-unsaturated *O*-methoxycarbonyl or *O*-pentafluorobenzoyloxime afforded 3,4-dihydro-2*H*-pyrroles using CuBr·Me$_2$S as the catalyst.[47] They also discovered the cyclization of *β*-(3-indolyl) ketone *O*-pentafluorobenzoyloximes to generate 3,4-dihydro-α-carbolines (Scheme 34).[48]



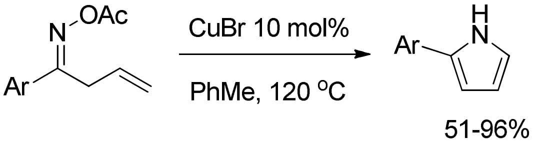
Scheme 34 Copper-catalyzed intramolecular amination of γ, δ-unsaturated oxime esters

Bower and coworkers recently reported the intramolecular amination of allylic C-H bond. The copper-catalyzed azo-Heck cyclization of oxime esters afforded pyrrolidine derivatives (Scheme 35).[49] Mechanistic studies indicated a reaction pathway proceeding *via* the generation and cyclization of an intermediate that possesses iminyl radical character.



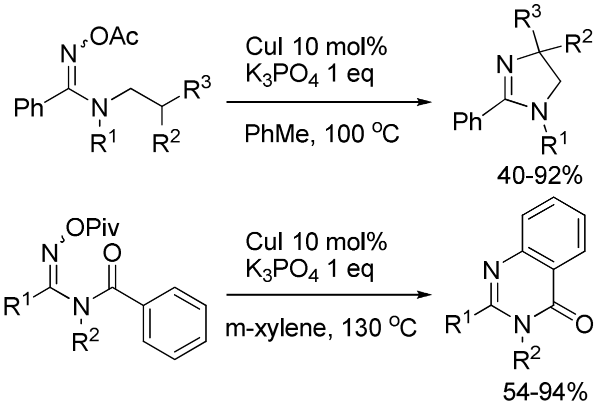
Scheme 35 Cu(2-ethylhexanoate)$_2$-catalyzed intramelecular amination of γ, δ-unsaturated oxime esters

Guan and coworkers reported a copper-catalyzed 5-endo-trig cyclization of β, γ-unsaturated ketoxime carboxylates for the synthesis of 2-arylpyrroles (Scheme 36).[50] This reaction tolerates a range of functional groups and is a practical procedure for rapid synthesis of 2-arylpyrroles.



Scheme 36 CuBr-catalyzed intramelecular amination of β, γ-unsaturated oxime esters

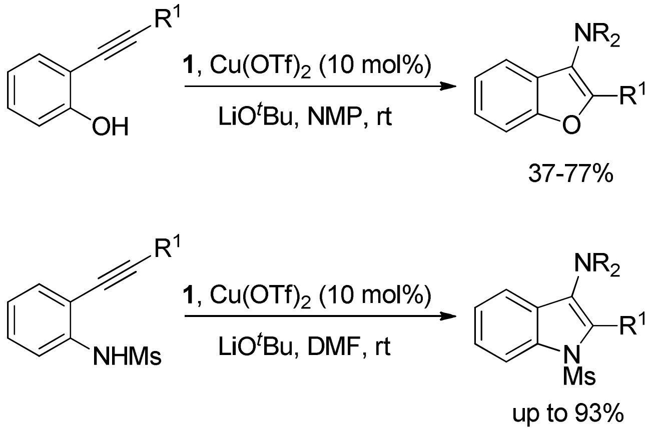
The intramolecular amination of amidoximes was recently investigated by Chiba's group. CuI-catalyzed reactions of *N*-alkylamidoximes afforded dihydroimidazoles via a sp^3 C-H amination. Reactions of *N*-benzoylamidoximes resulted in sp^2 C-H amination forming quinazolinones (Scheme 37).[51]



Scheme 37 CuI-catalyzed intramelecular amination of amidoximes

5. Annulative electrophilic amination of *o*-alkynylphenols and *o*-alkynylanilines

Metal-catalyzed electrophilic annulation of *o*-alkynylphenols and anilines was an efficient approach to constructing functionalized benzofurans and indoles. Muira and coworkers developed an effective copper-catalyzed annulative amination of *ortho*-alkynylphenols with *O*-benzoylhydroxylamines. The system may compensate for the precedents and provide a facile new route for the 3-aminobenzofuran skeletons of biological and pharmaceutical interest.[52] The annulative amination of *o*-alkynylanilines afforded the corresponding 3-aminoindoles (Scheme 38).[53]



Scheme 38 Cu(OTf)$_2$-catalyzed annulative amination of *o*-alkynylphenols and

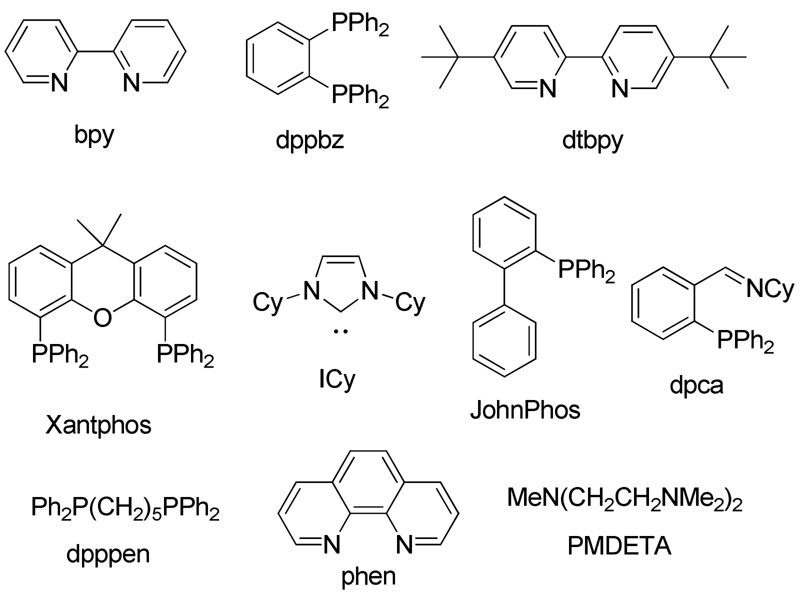
o-alkynylanilines

6. Conclusions and outlook

Copper-mediated electrophilic amination of organometallic reagents is an important and useful synthetic method for the preparation of aliphatic, aromatic, heteroaromatic amines as well as enamines and enamides and is continuing to gain the attentions of chemists. Furthermore, copper-catalyzed direct C-H amination with electrophilic aminating reagents provides a new and potentially more effective C-N bond formation approach for the synthesis of aromatic and heteroaromatic amines. We hope this perspective reflected the rapid development of interest in this field. Further work is needed to extend the scope of the organometallic reagents, direct C-H reagents as well as the electrophilic aminating reagents.

Abbreviations

Abbreviation of ligands involved in this perspective as shown in Scheme 39



Scheme 39 Ligands included abbreviation and structure in this perspective

Acknowledgments

This work was supported by the National Key Basic Research Program of China (973 program) (2012CB933402) and National Natural Science Foundation of China (Nos. 21272132 and 21032004).

References:

1. (a) T. Henkel, R. M. Brunne, H. Muller and F. Reichel, *Angew. Chem., Int. Ed.,* 1999, **38**, 643; (b) R. Hili and A. K. Yudin, *Nat. Chem. Biol.*, 2006, **2**, 284.

2. For recent reviews see: (a) D. S. Surry and S. L. Buchwald, *Chem. Sci.,* 2011, **2**, 27; (b) J. F. Hartwig, *Acc. Chem. Res.,* 2008, **41**, 1534; (c) D. S. Surry and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2008, **47**, 6338.

3. (a) F. Collet, R. H. Dodd and P. Dauban, *Chem. Commun.*, 2009, 5061; (b) F. Collet, C. Lescot and P. Dauban, *Chem. Soc. Rev.*, 2011, **40**, 1926; (c) J. L. Roizen, M. E. Harvey and J. Du Bois, *Acc. Chem. Res.*, 2012, **45**, 911; (d) A. N. Campbell and S. S. Stahl, *Acc. Chem. Res.*, 2012, **45**, 851; (e) R. T. Gephart and T. H. Warren, *Organometallics*, 2012, **31**, 7728; (f) M. Louillat and F. W. Patureau, *Chem. Soc. Rev.*, 2014, **43**, 901.

4. (a) D. M. T. Chan, K. L. Monaco, R.-P. Wang and M. P. Winters, *Tetrahedron Lett.*, 1998, **39**, 2933; (b) P. Y. S. Lam, C. G. Clark, S. Saubern, J. Adams, M. P. Winters, D. M. T. Chan and A. Combs, *Tetrahedron Lett.*, 1998, **39**, 2941; (c) D. A. Evans, J. L. Katz and T. R. West, *Tetrahedron Lett.*, 1998, **39**, 2937.

5. (a) J. Mulzer, H. J. Altenbach, M. Brown, K. Krohn and H. U. Reissi, *Organic Synthesis Highlights*. VCH: Weinhim, 1991, p. 45; (b) G. Boche, *Houben–Weyl, Methods of Organic Chemistry* (Eds.: G. Heimchen, R. W. Hoffman, J. Mulzer and E.

Schaumann), Vol. E21e. Thieme: Stuttgart, 1995, p. 5153; (c) A. Ricci, *Modern Amination Methods*.Wiley-VCH: Weinheim, 2000; (d) E. Ciganek, *Organic Reactions,*(Editor: Denmark, S. E.) Vol. 72, John Wiley & Sons, Inc., 2009, p. 1. (e) E. Erdik and M. Ay, *Chem. Rev.*, 1989, **89**, 1947; (f) T. Daskapan, *ARKIVOC*, 2011, 230; (g) T. J. Barker and E. R. Jarvo, Synthesis, 2011, **24**, 3954.

6. A. M. Berman and J. S. Johnson, *J. Org. Chem.*, 2006, **71**, 219

7. A. J. Biloski and B. Ganem, *Synthesis,* 1983, 537.

8. C. A. Broka and K. K. Eng, *J. Org. Chem.*, 1986, **51**, 5043

9. Y. Zhong, H. Zhou, D. R. Gauthier, J. Lee, D. Askin, U. H. Dolling and R. P. Volante, *Tetrahedron Lett.*, 2005, **46**, 1099.

10. S. Liu, Y. Yu and L. S. Liebeskind, *Org. Lett.*, 2007, **9**, 1947.

11. M. J. Campbell and J. S. Johnson, *Org. Lett.*, 2007, **9**, 1521.

12. E. Erdik and M. Ay, *Synth. React. Inorg. Met-Org.,* 1989, **19**, 663.

13. (a) H. Tsutsui, Y. Hayashi and K. Narasaka, *Chem. Lett.*, 1997, **26**, 317; (b) M. Kitamura, S. Chiba and K. Narasaka, *Bull. Chem. Soc. Jpn.*, 2003, **76**, 1063; (c) K. Narasaka, Pure Appl. Chem., 2002, **74**, 143.

14. P. Knochel and R. D. Singer, *Chem. Rev.*, 1993, **93**, 2117.

15. (a) G. H. Coleman, H. P. Andersen and J. L. Hermanson, *J. Am. Chem. Soc.*, 1934, **56**, 1381; (b) G. H. Coleman, J. L. Hermanson and H. L. Johnson, *J. Am. Chem. Soc.*, 1937, **59**, 1896.

16. A. M. Berman and J. S. Johnson, *J. Am. Chem. Soc.*, 2004, **126**, 5680.

17. A. M. Berman and J. S. Johnson, *J. Org. Chem.*, 2005, **70**, 364.

18. Berman, A. M.; Johnson, J. S. *Org. Synth.*, 2006, **83**, 31.

19. (a) T. Daşkapan, *Tetrahedron Lett.*, 2006, **47**, 2879; (b) T. Daşkapan, F. Yeşilbağ and S. Koca, *Appl. Organomet. Chem.*, 2009, **23**, 213.

20. T. Daşkapan and S. Koca, *Appl. Organomet. Chem.*, 2010, **24**, 12.

21. S. L. McDonald, C. E. Hendrick and Q. Wang, *Angew. Chem. Int. Ed.*, 2014, **53**, 4667.

22. S. L. McDonald and Q. Wang, *Angew. Chem. Int. Ed.*, 2014, **53**, 1867.

23. S. L. McDonald and Q. Wang, *Chem. Commun.*, 2014, **50**, 2535.

24. (a) D. G. Hall in *Boronic acids,Vol. 1* (Ed.: D. G. Hall), Wiley-VCH, Weinheim, 2011; (b)) N. Miyaura and A. Suzuki, *Chem. Rev.,* 1995, **95**, 2457; (c) S. Kotha, K. Lahiri and D. Kashinath, *Tetrahedron,* 2002, **58**, 9633.

25. N. Matsuda, K. Hirano, T. Satoh and M. Miura, *Angew. Chem. Int. Ed.*, 2012, **51**, 3642.

26. T. Ishiyama, J. Takagi, K. Ishida, N. Miyaura, N. R. Anastasi and J. F. Hartwig, *J. Am. Chem. Soc.*, 2002, **124**, 390.

27. R. P. Rucker, A. M. Whittaker, H. Dang and G. Lalic, *Angew. Chem. Int. Ed.*, 2012, **51**, 3953.

28. R. P. Rucker, A. M. Whittaker, H. Dang and G. Lalic, *J. Am. Chem. Soc.*, 2012, **134**, 6571.

29. R. Sakae, K. Hirano, T. Satoh and M. Miura, *Chem. Lett.*, 2013, **42**, 1128.

30. Z. Zhang, Y. Yu and L. S. Liebeskind, *Org. Lett.*, 2008, **10**, 3005.

31. C. He, C. Chen, J. Cheng, C. Liu, W. Liu, Q. Li and A. Lei, *Angew. Chem.*

Int. Ed., 2008, **47**, 6414.

32. S. Liu, Y. Yu and L. S. Liebeskind, *Org. Lett.*, 2007, **9**, 1947.

33. S. Liu and L. S. Liebeskind, *J. Am. Chem. Soc.*, 2008, **130**, 6918.

34. (a) P. Y. S. Lam, S. Deudon, K. M. Averill, R. Li, M. Y. He, P. DeShong and C. G. Clark, *J. Am. Chem. Soc.*, 2000, **122**, 7600; (b) P. Y. S. Lam, S. Deudon, E. Hauptman and C. G. Clark, *Tetrahedron Lett.*, 2001, **42**, 2427.

35. (a) R.-J. Song, C.-L. Deng, Y.-X. Xie and J.-H. Li, *Tetrahedron Lett.*, 2007, **48**, 7845; (b) B. Lin, M. Liu, Z. Ye, J. Ding, H. Wu and J. Cheng, *Org. Biomol. Chem.*, 2009, **7**, 869.

36. Y. Miki, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2013, **15**, 172.

37. M. H. Nguyen and A. B. Smith, *Org. Lett.*, 2013, **15**, 4872.

38. N. Matsuda, K. Hirano, T. Satoh and M. Miura, *Angew. Chem. Int. Ed.*, 2012, **51**, 11827.

39. T. Miura, M. Morimoto and M. Murakami, *Org. Lett.*, 2012, **14**, 5214.

40. T. J. Barker and E. R. Jarvo, *Angew. Chem. Int. Ed.*, 2011, **50**, 8325.

41. X. Yan, C. Chen, Y. Zhou and C. Xi, *Org. Lett.*, 2012, **14**, 4750.

42. H. Liu, X. Yan, C. Chen, Q. Liu and C. Xi, *Chem. Commun.*, 2013, **49**, 5513.

43. H. Liu, Y. Zhou, X. Yan, C. Chen, Q. Liu and C. Xi, *Org. Lett.*, 2013, **15**, 5174.

44. Y. Zhou, X. Yan, C. Chen and C. Xi, *Organometallics*, 2013, **32**, 6182.

45. T. Kawano, K. Hirano, T. Satoh and M. Miura, *J. Am. Chem. Soc.*, 2010, **132**, 6900.

46. N. Matsuda, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2011, **13**, 2860.

47. Y. Koganemaru, M. Kitamura and K. Narasaka, *Chem. Lett.*, 2002, **31**, 784.

48. K. Tanaka, M. Kitamura and K. Narasaka, *Bull. Chem. Soc. Jpn.,* 2005, **78**, 1659.

49. A. Faulkner, N. J. Race, J. S. Scott and J. F. Bower, *Chem. Sci.*, 2014, **5**, 2416.

50. W. Du, M. Zhao, Z. Ren, Y. Wang and Z. Guan, *Chem. Commun.*, 2014, **50**, 7437.

51. H. Chen and S. Chiba, *Org. Biomol. Chem.*, 2014, **12**, 42

52. K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2011, **13**, 2395.

53. N. Matsuda, K. Hirano, T. Satoh and M. Miura, *J. Org. Chem.*, 2012, **77**, 617.