Topics in Current Chemistry (2023) 381:4
https://doi.org/10.1007/s41061-022-00414-5

REVIEW

O-Benzoylhydroxylamines: A Versatile Electrophilic Aminating Reagent for Transition Metal-Catalyzed C–N Bond-Forming Reactions

Sachin Balaso Mohite[1] · Milan Bera[2] · Vishal Kumar[1] · Rajshekhar Karpoormath[1] · Shaik Baji Baba[1] · Arjun S. Kumbhar[3]

Received: 4 July 2022 / Accepted: 16 November 2022

Abstract

Owing to the prevalence of nitrogen-containing compounds in natural products and important pharmaceutical agents, chemists, have actively searched for the development of efficient and selective methodologies allowing for the facile construction of carbon–nitrogen bonds. Over the last decade, transition metal-catalyzed C–N bond construction via electrophilic amination reaction has emerged as an attractive approach for the synthesis of various organic molecules and pharmaceuticals. Particularly, *O*-benzoylhydroxylamines as an electrophilic aminating agent have proven to be the best and most widely used in both academic and industrial research. In this review, we highlight the key contributions to the recent transition metal-catalyzed C–N bond formation reactions using *O*-benzoylhydroxylamines as an aminating agent and their relevant mechanistic insights.

✉ Rajshekhar Karpoormath
karpoormath@ukzn.ac.za

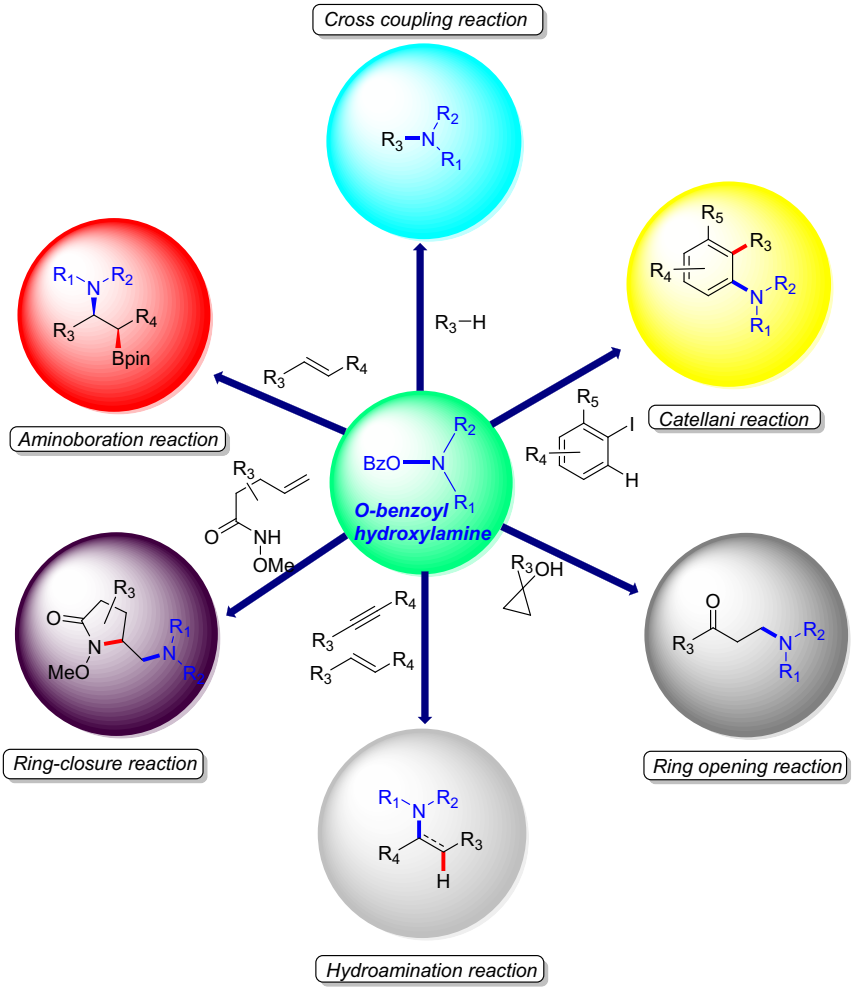
[1] Department of Pharmaceutical Chemistry, Discipline of Pharmaceutical Sciences, College of Health Sciences, University of KwaZulu-Natal (Westville), Durban 4000, South Africa

[2] Department of Chemistry, Chung-Ang University, 84 Heukseok-ro, Dongjak-gu, Seoul 06974, Republic of Korea

[3] Department of Chemistry, Vivekanand College, Kolhapur (Autonomous), Maharastra 416003, India

Published online: 18 December 2022

Graphical Abstract



Keywords *O*-Benzoylhydroxylamine · Electrophilic amination · Transition metal catalysis · Cross-coupling · Aminoboration · Hydroamination

1 Introduction

The carbon–nitrogen (C–N) chemical linkage is one of the fundamental bonds, widely present in various value-added products such as pharmaceuticals, synthetic intermediates, natural products, coordinating ligands, etc. [1–5]. C–N bonds are typically formed via a nucleophilic substitution (SN_2) attack of nucleophilic nitrogen on an electrophilic carbon or a reductive amination. Various limitations

exist, however, especially in substrate scope with diverse functionalities [6, 7]. Several synthetic routes have been proposed to address these challenges, such as transition-metal-catalyzed cross-coupling reactions [8], especially Ullman–Goldberg [9, 10], and Buchwald–Hartwig [11, 12] type amination/amidation reactions (Fig. 1, route A), C–H nitrogen insertion [13], enzymatic reactions [14, 15], and nucleophilic addition to imines.

The transformation of the C–H bond into a C–N bond has great significance in synthetic chemistry. Especially, the formation of C–N bond via oxidative C–H and N–H cross-coupling processes in the presence of transition metal catalysis has been also standing as a significant and effective strategy for the synthesis of various amines [16–18] (Fig. 1, route B). On the other hand, an umpolung strategy-electrophilic amination has remained an attractive area in this field using an R_2N^+ type electrophilic reagent in which R_2N^+ is incorporated as a nitrogen source (Fig. 1, route C) [19].

Among the various modern synthetic strategies, electrophilic amination is an important and unconventional C–N bond formation process in organic synthesis. To date, many electrophilic aminating reagents have been developed and used in amination reactions (Fig. 2) [20, 21]. Among all of these electrophilic amination reagents, *O*-benzoylhydroxylamines are the most convenient and broadly used electrophilic aminating reagents [22]. Furthermore, these reagents have many advantages, such as being easy to synthesize, easy availability, high stability, and excellent reactivity in transition metal-catalyzed C–N bond formation reactions. Additionally, electrophilic amination reactions using *O*-benzoylhydroxylamines have rapidly evolved and have made some breakthroughs in organic transformation [23]. The present review aims to highlight the recent advances in C–N bond

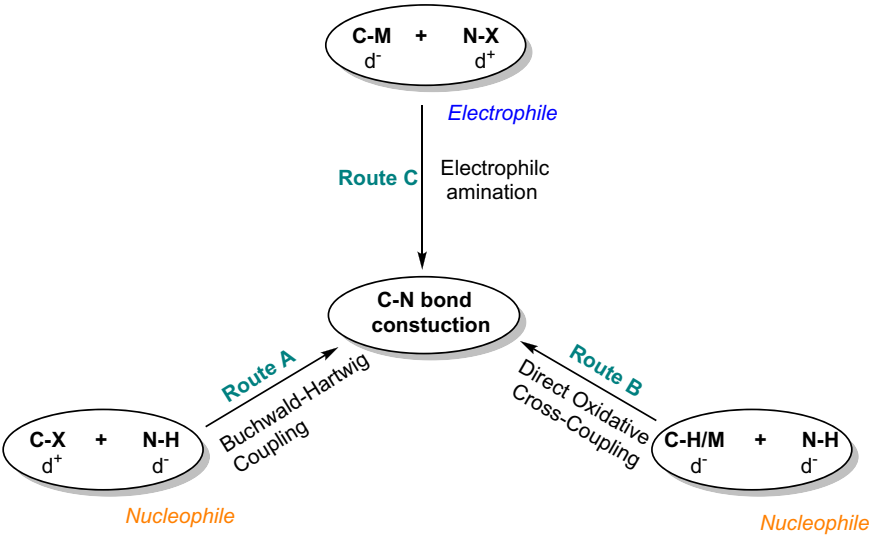


Fig. 1 C–N bond formation via cross-coupling reactions

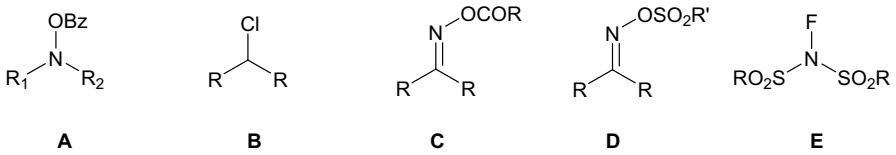


Fig. 2 Typical electrophilic aminating agents

formation strategies using *O*-benzoylhydroxylamines an electrophilic aminating reagent, covering the period from 2016 to the present day.

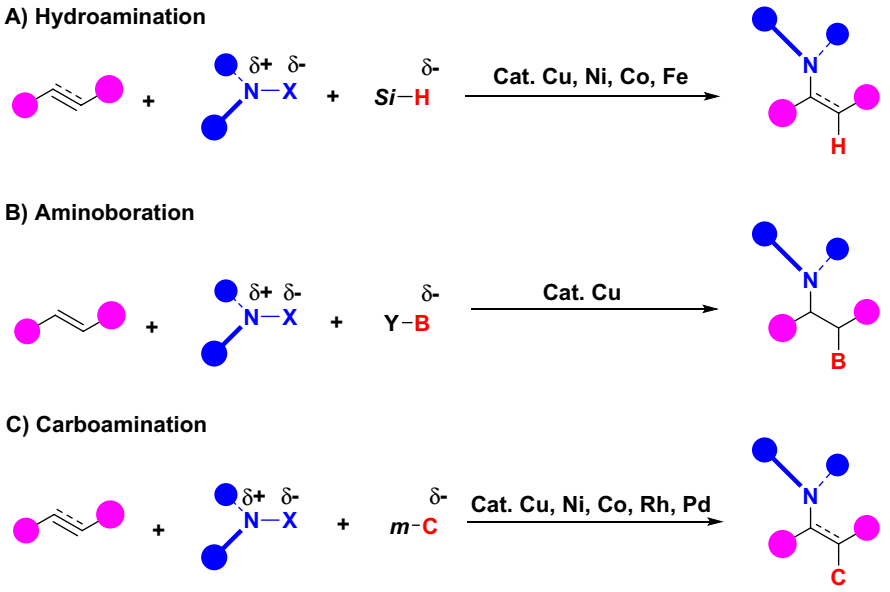
2 Transition Metal-Mediated Approaches

The development of methods for introducing nitrogen functionality into organic frameworks is one of the major research topics in synthetic chemistry [24–27]. A large number of amino functionalities are present in different natural products, synthetic intermediates, and pharmaceutical agents, while traditional approaches to constructing carbon–nitrogen bonds often require several steps. Hence, metal-mediated C–N bond formation has opened a new avenue regarding efficiency and applicability. Aside from seminal reports on the transition metal-catalyzed C–N bond formation via cross-coupling reactions, especially Ullman–Goldberg, and Buchwald–Hartwig amination reactions, independently developed transition metal-catalyzed electrophilic amination procedures with the help of suitable electrophilic aminating agents. This method has been significantly advanced during the past decades and is now considered one of the most reliable synthetic routes for the construction of C–N bonds. Among the electrophilic aminating reagents, *O*-benzoylhydroxylamines have received the greatest attention and have been used in a variety of aminations, particularly in transition metal-catalyzed processes [28–30]. In this regard, this comprehensive review explored the use of Cu, Pd, Ni, and Co-catalyzed electrophilic aminations using *O*-benzoylhydroxylamines as an electrophilic aminating reagent (Scheme 1).

2.1 Amination of Alkenes and Alkynes

2.1.1 Hydroamination

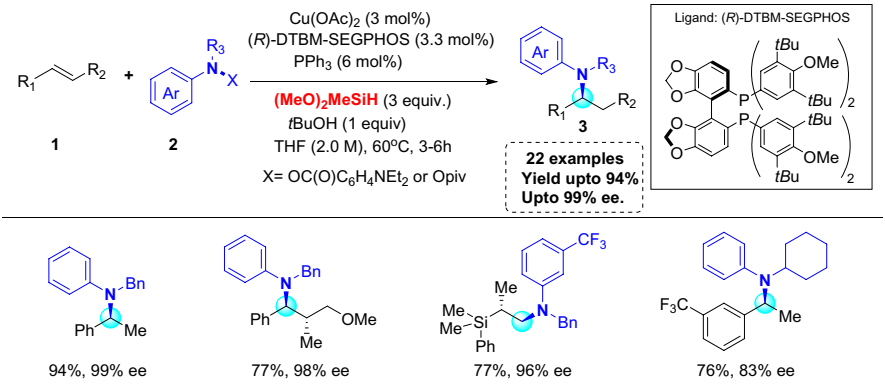
The net hydroamination of alkenes via the umpolung electrophilic amination strategy was first reported by Hirano/Miura group [37] and Buchwald group [38] using *O*-benzyl hydroxylamine and hydrosilane as a hydrogen source. Later, the same groups [38–41] developed newer and superior hydroamination methods. To complement this some new results and more particular, mechanisms of the reactions are discussed in the following section.



Scheme 1 Umpolung-enabled three-component-coupling type aminofunctionalizations of alkenes and alkynes

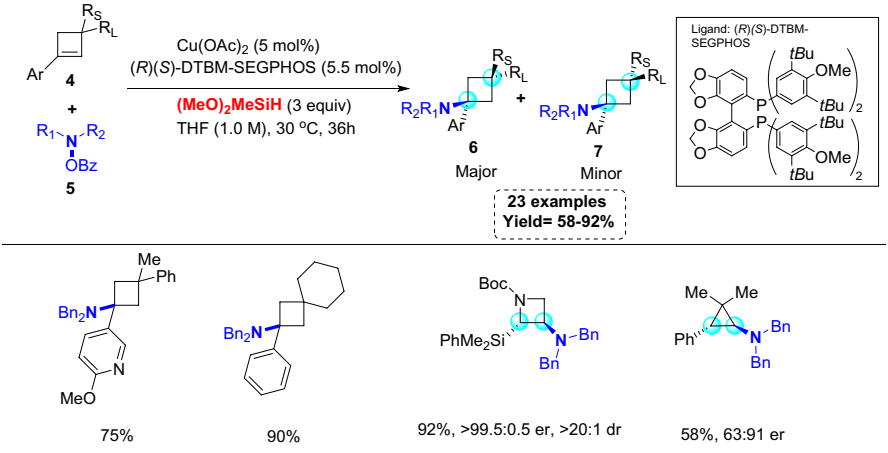
2.1.1.1 Cu Catalyst Cu salts catalyzed net hydroamination of alkenes and alkynes with silane and electrophilic amination reagents or amine transfer reagents (R_2N-OBz) is a straightforward method for obtaining chiral amines. The scope of previously employed electrophilic aminating agents or hydroxylamines was confined to *N*,*N*-dialkyl derivatives, but the suitable amendment in leaving group successfully broadened their scope. Additionally, the decomposition of amine derivatives with CuH species has predominantly happened in the case of *N*,*N*-dialkyl hydroxylamine derivatives. The Buchwald group described a modified method in 2015, in which the diethylamino group was introduced at the *para* position of the benzoate leaving moiety. This alteration resulted in a significant improvement in stability and reactivity, allowing for the net hydroamination of secondary and tertiary amines [42].

Simple styrene, cinnamyl alcohol/amine, and its cyclic derivatives have been found viable substrates for electrophilic hydroamination. The construction of biologically important chiral *N*-arylamines (**3**) using modified electrophilic reagent and reaction conditions (*N*-hydroxylamine ester) was reported by Ichikawa et al. [43]. They observed the reduction of *N*-hydroxylamine ester with CuH catalyst in prior work, thus they improved the approach to allow secondary anilines to be installed across the double bonds of styrene, 1,1 disubstituted alkene, and unactivated terminal alkenes (**1**). The NMR studies indicated that the addition of *t*BuOH and PPh_3 additives might reduce the unproductive reduction of *N*-hydroxylamine ester (**2**) and play a crucial role in this transformation. This modification resulted in a dramatic increase in reactivity and yield (Scheme 2).

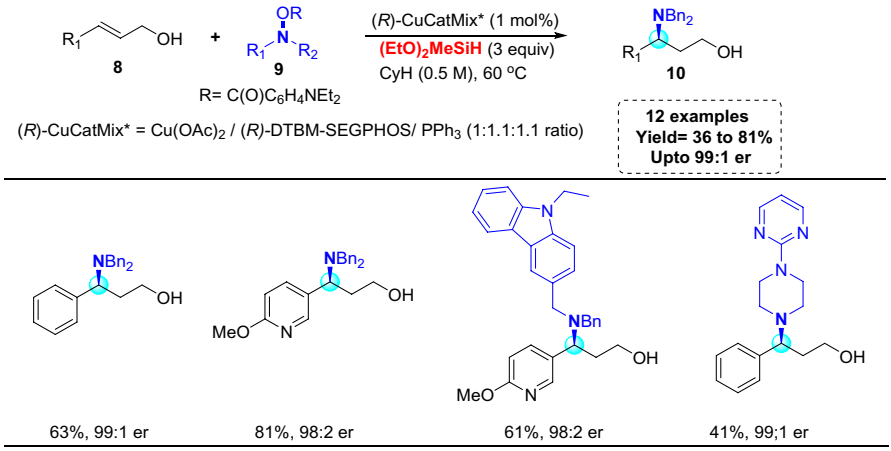


Scheme 2 Cu (II)-catalyzed net hydroamination of 1,1 disubstituted alkene and unactivated terminal alkenes

Despite significant progress in Cu-catalyzed hydroamination methods, stereoselective hydroamination of strained unactivated alkenes remains a challenge. Because of the common stumbling blocks in these reactions, such as electrophile reduction with catalyst and the high barrier to reaction with CuH (hydrocupration). In this regard, the Cu(II)/(*R*)-DTBM-SEGPHOS-catalyzed diastereo- and enantioselective hydroamination of 1-substituted cyclobutenes (**4**) and cyclopropenes was reported by the Buchwald group in 2019 [44] (Scheme 3). The DFT calculations demonstrated that strained unactivated alkenes have a faster rate of hydrocupration than unstrained unactivated alkenes, allowing for hydroamination. 1-aryl cyclobutenes delivered the desired product with Markovnikov selectivity



Scheme 3 Buchwald's Cu(II)/(*R*)-DTBM-SEGPHOS-catalyzed diastereo- and enantioselective hydroamination of 1-substituted cyclobutenes and cyclopropenes

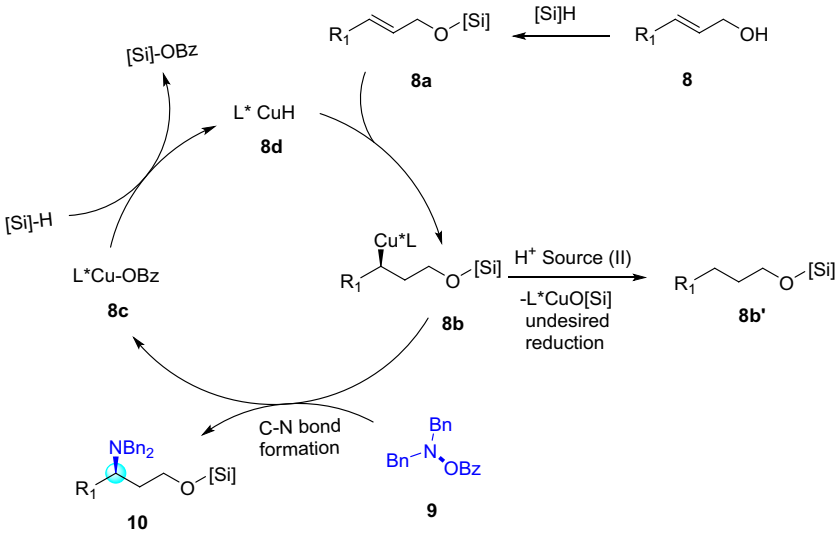


Scheme 4 Buchwald's enantioselective hydroamination of allyl alcohols

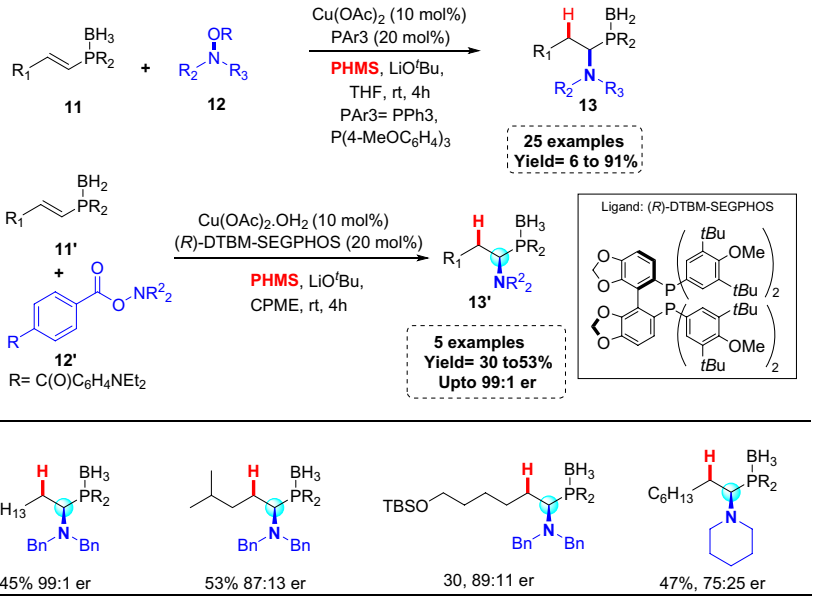
and formation of tetrasubstituted carbon in the 1-aryl cyclobutene product. However, in the case of 1-aryl cyclopropene derivatives, the opposite results (anti-Markovnikov selectivity) were observed, which could be because selectivity for 1-aryl cyclobutene derivatives was controlled by distortion energy in the hydrocupration transition state, whereas selectivity for 1-aryl cyclopropene derivatives was controlled by substrate–catalyst interaction. The key advantages of this reaction are broad substrate scope, good functional group tolerance, and excellent stereoselectivity.

In the same year, they developed the one-step method for the synthesis of enantioselective α-amino alcohols (**10**) from the unprotected allyl alcohols (**8**) and hydroxylamine ester (**9**) [45] (Scheme 4). The optimization studies suggested that the undesired product formation, particularly the reduction of allyl alcohol substrate can be controlled by using an appropriate solvent. Also, the exclusive formation of enantioselective α-amino alcohols instead of β-amino alcohols was due to the generation of more stable benzylic copper species in the hydrocupration step. The enantioselectivity-determining procedure could be explained by the proposed reaction mechanism in Scheme 5. The dehydrogenative silylation between allylic alcohol (**8**) and silane gives silyl protected allyl alcohol (**8a**). Subsequent hydrocupration of silyl protected allyl alcohol (**8a**) afforded chiral alkyl copper species (**8b**), followed by electrophilic amination with hydroxylamine (**9**) ester delivered the desired enantioselective α-amino alcohol product (**10**).

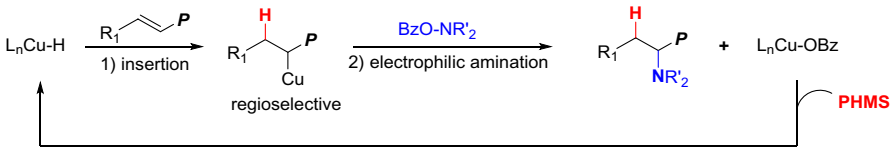
In 2019, Takata et al. [46] reported the hydroamination of vinyl phosphine borane (**11**) to afford medicinally and pharmaceutically important regioselective *α*-amino phosphine boranes (**13**) (Scheme 6). The regioselectivity was achieved by screening different biphoshine ligands and solvents, with the $Cu(OAc)_2 \cdot OH_2$/(R)-DTBM-SEGPHOS catalyst and the CPME solvent proving to be the most effective. The working hypothesis for the catalytic cycle of net hydroamination of vinyl phosphine borane includes in situ generation of Cu–H species, alkenes insertion to the Cu–H species



Scheme 5 Proposed reaction mechanism of Buchwald's enantioselective hydroamination of allyl alcohols



Scheme 6 Miura's hydroamination of vinyl phosphine borane to afford medicinally and pharmaceutically important regioselective α-amino phosphine



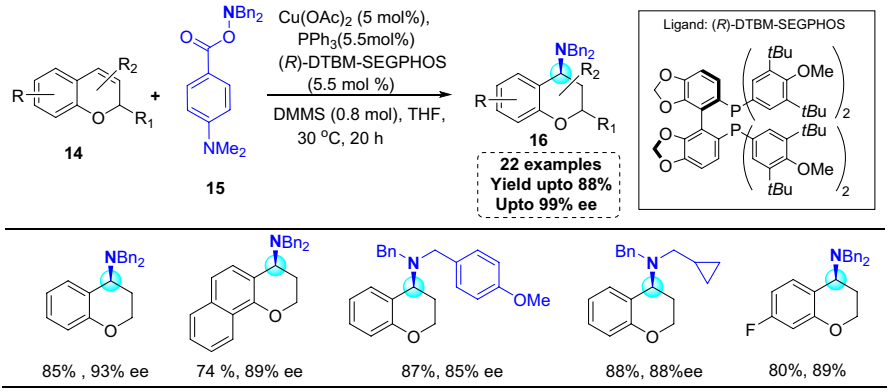
Scheme 7 The working hypothesis of Miura's hydroamination method

generating alkyl copper intermediate, and electrophilic trapping with hydroxylamine (Scheme 7).

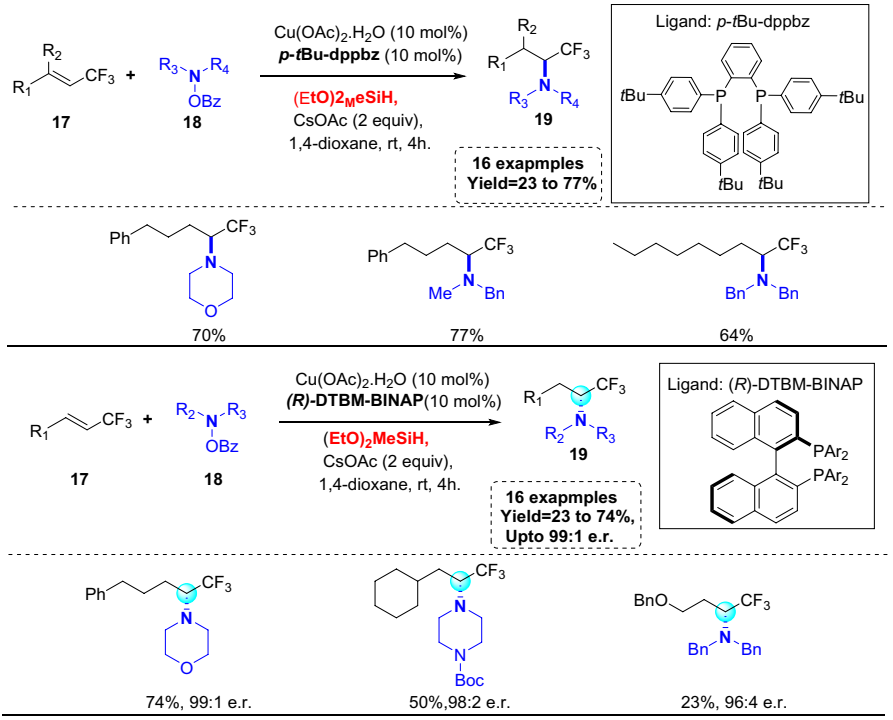
Chromene scaffold is a privileged structural motif found in many natural products and bioactive compounds. Wang's group [47] reported Cu/(*R*)-DTBM-SEGPHOS-catalyzed asymmetric hydroamination of *2H*-chromenes (**14**) to afford optically enriched 4-amino chromenes (**16**) (Scheme 8). The appropriate 4-amino chromene (**16**) derivatives were produced in good yield with excellent enantioselectivity using this procedure, which exhibited high functional group compatibility. Furthermore, both cyclic and acyclic *O*-benzylhydroxylamine (**15**) derivatives underwent the reaction smoothly.

A Cu-catalyzed, regio- and enantioselective electrophilic amination of 1-trifluoromethyl alkenes (**17**) were developed by Miura et al. [48]. The reaction was performed in presence of Cu $(OAc)_2 \cdot H_2O$ (10 mol%) catalyst, *p-t*Bu-dppbz (10 mol%) ligand, and CsOAc (2 equiv.) base, afforded corresponding hydroaminated product (**19**) was obtained in moderate-to-good yields (23–77%) (Scheme 9). Remarkably, the use of the (*R*)-DTBM-BINAP instead of p-*t*Bu-dppbz ligand resulted in excellent regio and enantioselectivity. This suggests that a precise ligand selection could prevent unwanted *β*-F elimination, specifically the biphosphine ligand-bearing electron-rich group on *ortho-* and *-meta* positions. Differently substituted trifluoromethyl alkene (**17**) and *O*-benzoylhydroxylamines (**18**) could be accepted.

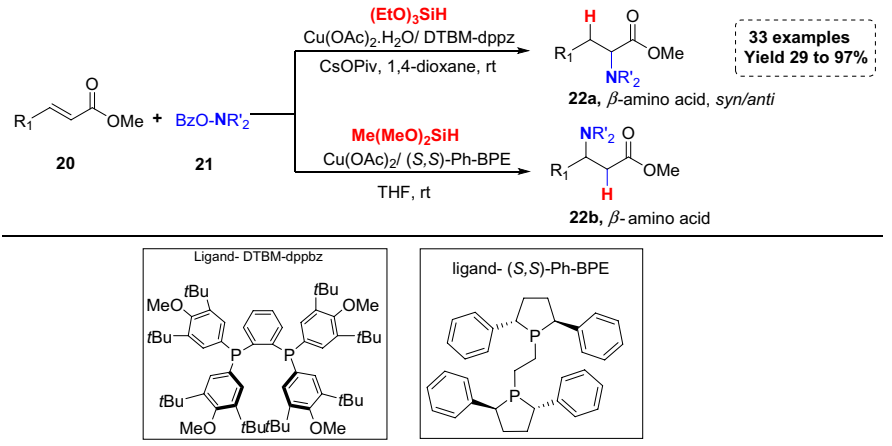
In 2021, Nishino et al. [49] demonstrated the net hydroamination of *α,β*-unsaturated ester (**20**) with hydrosilane and hydroxylamine (**21**) to afford corresponding medicinally significant *α*-amino acid (**22a**) and *β*-amino acid derivatives



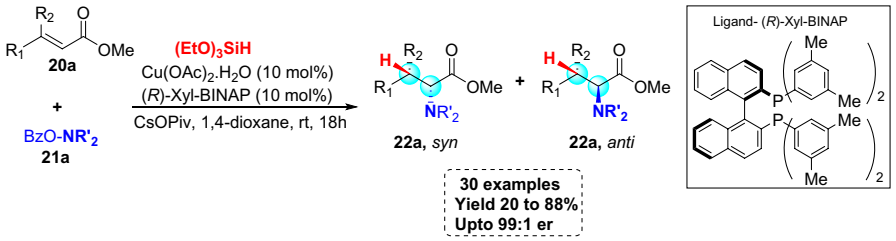
Scheme 8 Wang's Cu/(*R*)-DTBM-SEGPHOS-catalyzed asymmetric hydroamination of *2H*-chromenes



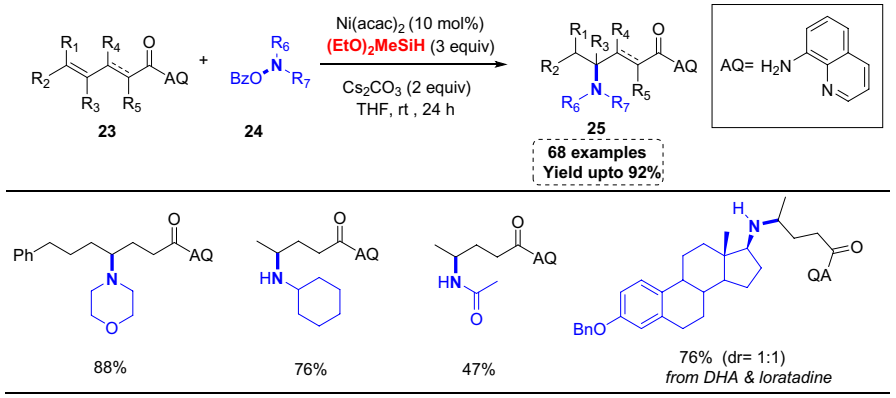
Scheme 9 Cu(II)-catalyzed electrophilic amination of trifluoromethyl alkenes



Scheme 10 Cu-catalyzed net hydroamination of α,β-unsaturated ester



Scheme 11 Enantioselective hydroamination of β,β-disubstituted α,β-unsaturated ester

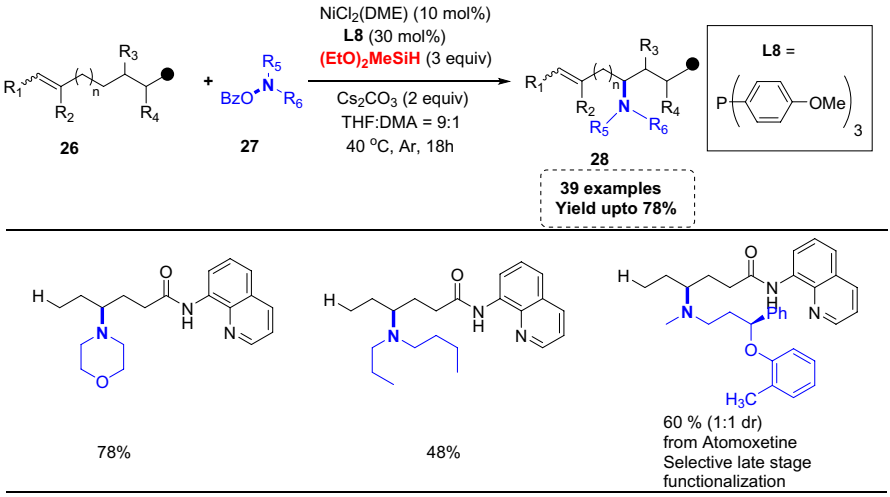


Scheme 12 Ni-catalyzed selective hydroamination of the terminal and internal unactivated alkenes

(**22b**) (Scheme 10). Condition-dependent regiodivergency was seen in this transformation; in the case of the $Cu(OAc)_2H_2O$/DTBM-dppbz catalytic system, the α-amino acid (**22a**) product was generated exclusively, whereas the $Cu(OAc)_2$/(*S, S*)-Ph-BPE catalytic system provided the β-amino acid derivative (**22b**) selectively. Furthermore, the control experiments suggested that the appropriate base CsOPiv and remote steric hindrance bearing DTBM-dppbz ligand allows challenging C–N bond formation at the α-position of a carbonyl group. Likewise, the chiral ligands Xyl-BINAP or DTBM-SEGPHOS, which have comparable distant steric bulkiness, successfully control chirality at the β-position.

The attempts at asymmetric induction at the α-position were unsuccessful in the earlier example. However, the β,β-disubstituted substrate (**20a**) was converted to the optically active (**22a**) with high enantioselectivity but moderate diastereoselectivity using the (*R*)-Xyl-BINAP chiral ligand. This indicates that in the olefin insertion step, effective asymmetric induction occurs at the β-position, but the generated copper enolate undergoes electrophilic amination at the α-position with poor diastereoselectivity (Scheme 11).

2.1.1.2 Ni Catalyst The selective hydroamination of the terminal and internal unactivated alkenes (**23**) to construct relative β- and γ-aminated products (β- and

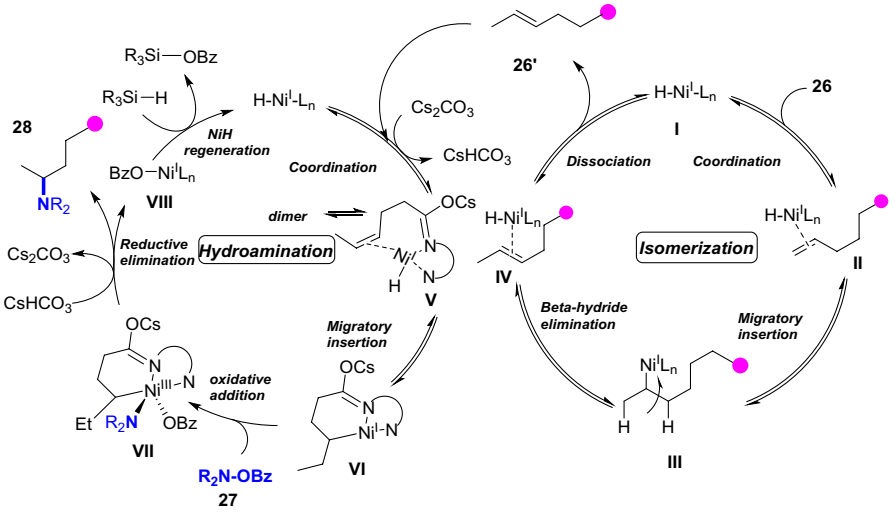


Scheme 13 Hong's selective and migratory hydroamination strategy

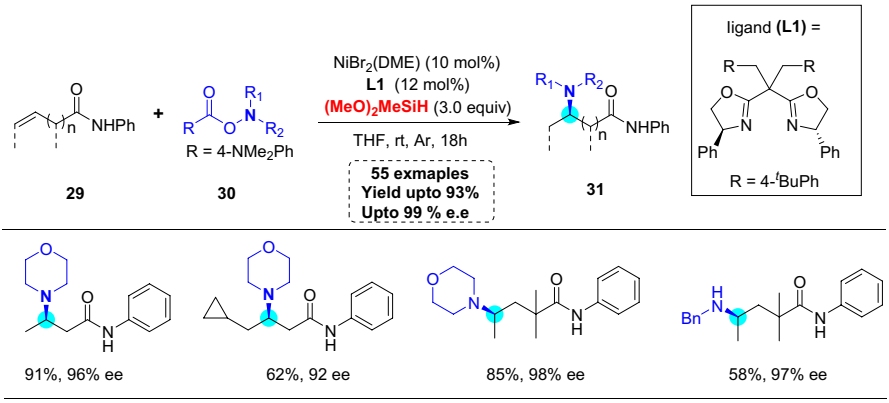
γ-amino acid derivatives) (**25**) under the Ni catalyst was demonstrated by Hong et al. [50] (Scheme 12). Notably, the regioselective *syn* isomeric product was obtained in the case of internal alkenes and the stereochemistry was confirmed by X-ray crystallographic analysis. The results of this study concluded that the coordination of the directing group to the nickel hydride intermediate in the alkene migratory insertion stage via the inner-sphere installation of the amino group determines the *syn*-configuration. Further, the synthetic utility of this transformation was validated by site-selective late functionalization of the medicinally significant complex molecules.

In 2021, the same group extended their methodology to more functionalized unactivated alkenes (**26**) via selective and migratory hydroamination strategy to incorporate various amino groups on (sp3) C of long aliphatic chains (Scheme 13) [51]. This transformation delivered selective γ-aminated (**28**) products with excellent regioselectivity. The selectivity could be achieved at the migratory insertion stage by stabilizing the six-membered nickelacycle and directing the group complex, which further proceeds through oxidative addition followed by reductive elimination. Furthermore, the selective δ-amination was accomplished by employing picolinamide as a directing group to the alkene.

Based on the previous literature and controlled studies a possible mechanistic pathway was proposed (Scheme 14). Firstly, the alkyl nickel hydride intermediate (**III**) was produced by the insertion of nickel (I) hydride (**I**) into the olefins, which were formed by the merger of nickel precatalyst and hydrosilane (**III**), which further generates isomeric γ, δ-alkene intermediate (**IV**). Subsequently, the migratory insertion step leads to the formation of nickelacycle (**V**). Finally, the stabilized directing group and nickel complex undergoes selective cross-coupled amination via oxidative



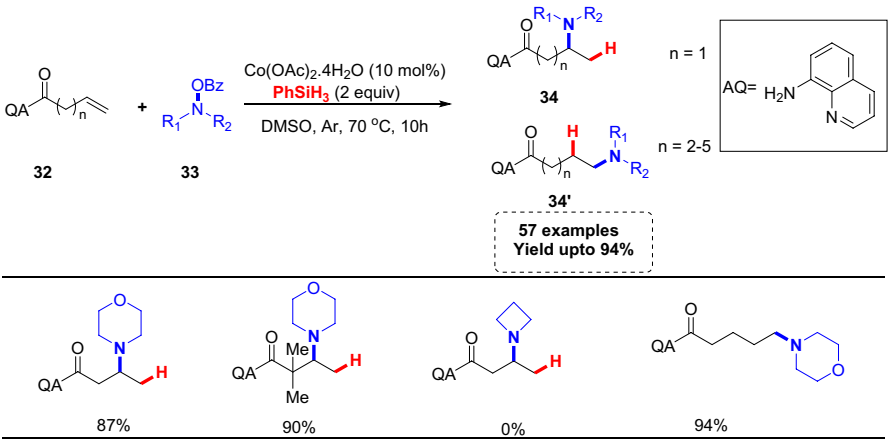
Scheme 14 Proposed reaction mechanism for Hong's selective and migratory hydroamination strategy



Scheme 15 Hong's Ni-catalyzed terminal and internal hydroamination of unactivated alkene

addition followed by reductive elimination to deliver the desired γ-aminated product along with BzO-Ni^{I}L$_n$ (**VIII**) and regeneration of the catalyst.

As a continuous work, the Hong group [52] described Ni-catalyzed terminal and internal hydroamination of unactivated alkene (**29**) bearing weakly coordinating amide or ester directing group with high enantio- and regioselectivity (Scheme 15). To improve the reactivity, and stereo selectivity series of modified bisoxazoline (BOX) chiral ligands and modified hydroxylamine ester was employed. The mechanistic studies indicated that chiral bisoxazoline-bound Ni species successfully exploit carbonyl coordination to accomplish enantio- and regioselective NiH insertion into alkenes. The key advantages of this unified



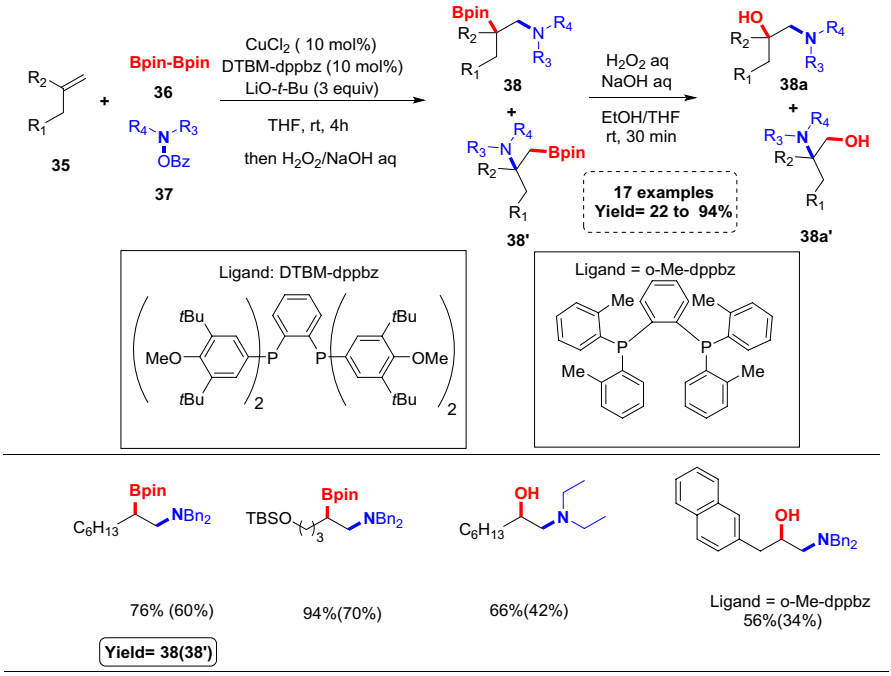
Scheme 16 Song and Niu's Co-catalyzed intramolecular hydroamination of unactivated alkene

transformation are broad substrate scope, mild reaction conditions, and excellent enantio- and regioselectivity.

2.1.1.3 Co Catalyst In the past two decades, intramolecular hydroamination of amino alkenes has received much attention and has shown remarkable progress. However, intermolecular hydroamination of unactivated alkenes is still challenging, especially using cobalt salts. In this regard, Song et al. [53] described the intramolecular hydroamination of unactivated alkene (**32**) bearing removable directing group. The reaction afforded corresponding regioselective amino acid derivatives (**34**) under earth-abundant and inexpensive cobalt metal catalyst (Scheme 16). Differently substituted unactivated alkenes, such as *β,γ*- and *γ,δ*-unactivated alkenes, as well as even more difficult long-chain alkenes were reacted and delivered relative products by following the Markovnikov and anti-Markovnikov rules.

2.1.2 Aminoboration

2.1.2.1 Cu Catalyst In 2013, Hirano and Miura's group reported the first example of Cu-catalyzed aminoboration, incorporating amino and boron groups simultaneously in a *syn* configuration to the styrenes [54]. In the following year, they came up with a modified synthetic protocol to achieve selective aminoboration of methyl cyclopropene [55] and dicycloalkenes [56]. In continuation of their work, they further developed a ligand-controlled regiodivergent Cu-catalyzed aminoboration of unactivated terminal alkenes to prepare *β*-borylalkylamines in the same year [57]. In 2016, the same group developed the second-generation Cu and modified bipohosphine ligand catalyst to achieve regioselective amino-boration of terminal unactivated alkenes (**35**) (Scheme 17) [58]. A series of biphosphine ligands were modified and examined to obtain the desired product with regioselectivity in good yields, confirming that the DTBM-dppbz ligand was most effective. This newly developed catalytic system could install a readily transformable Bpin group at the hindered position, which allows the



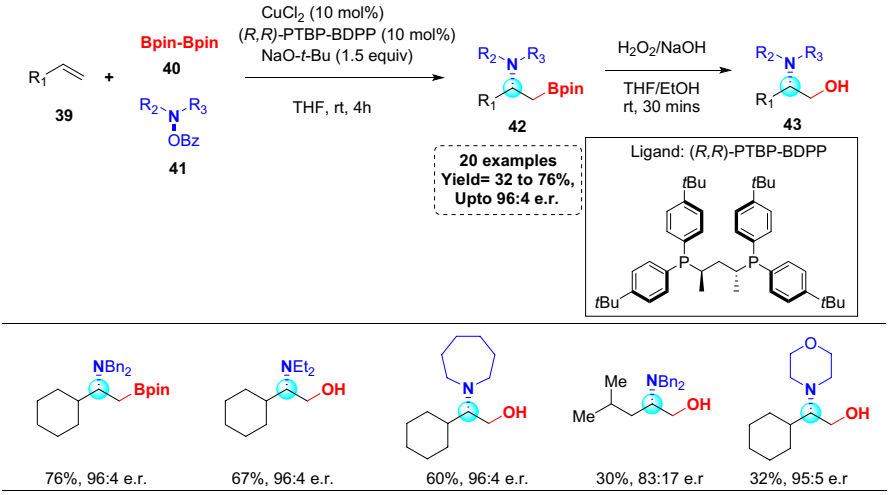
Scheme 17 Miura's Cu (II)-catalyzed aminoboration of unactivated terminal alkenes

aminoboration of the 1,1-disubstituted alkenes, which was previously inaccessible by using IPr-CuBr-based first-generation catalyst.

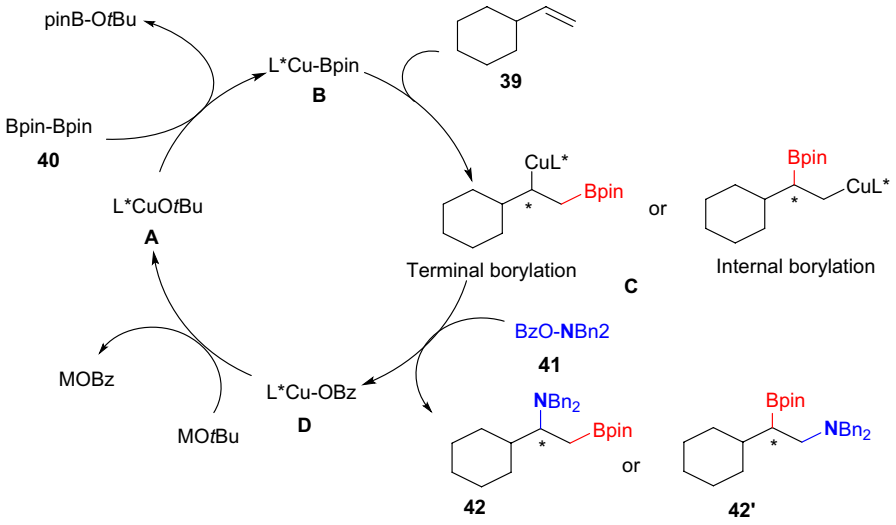
In the following year, the same group extended their methodology to a more functionalized terminal unactivated olefins (**39**) by employing modified reaction conditions such as the use of CuCl (10 mol%) as a catalyst and (*R, R*)-PTBP-BDPP (10 mol%) as a ligand. This modification enhanced the yield with regio- and enantioselectivity ratios [59]. The bulky *tert*-butyl group on the *para* position of (*R, R*)-PTBP-BDPP ligand is crucial in achieving high regio- and enantioselectivity. The regioselectivity was also dependent on the electronic and steric nature of hydroxylamine (**41**). The major advantage of this transformation is that it allows the incorporation Bpin group at the terminal position, which could be converted into many functionalities (Scheme 18).

The plausible reaction mechanism is depicted in Scheme 19. Firstly, the generation of active boryl species L*Cu-Bpin (**B**) via σ-bond metathesis between L*CuO*t*Bu (**A**) and Bpin-Bpin (**40**). Secondly, there is the formation of a C–N bond with hydroxylamine (**41**) via alkene (**39**) addition into L*Cu-Bpin (**B**), delivered the desired product (**42/42′**) and regeneration of L*CuO*t*Bu (**A**).

Liu et al. [60] developed an efficient approach for the synthesis of α-aminoboron derivatives (**47**) via CuH-catalyzed hydroamination/hydroboration of terminal alkynes (**44**). Remarkably, this organic transformation preferentially yields the desired 1,1-heterodifunctionalized products rather than the alternative homodifunctionalized, 1,2-heterodifunctionalized, or reductively monofunctionalized



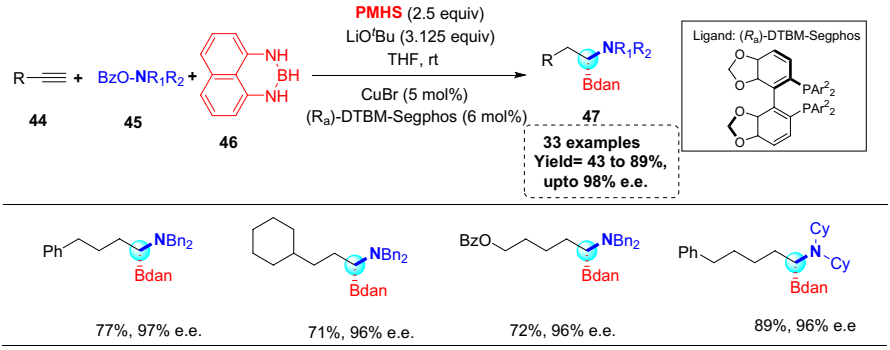
Scheme 18 Miura's developed Cu(II)-catalyzed regio-and enantioselective aminobortion of unactivated alkenes



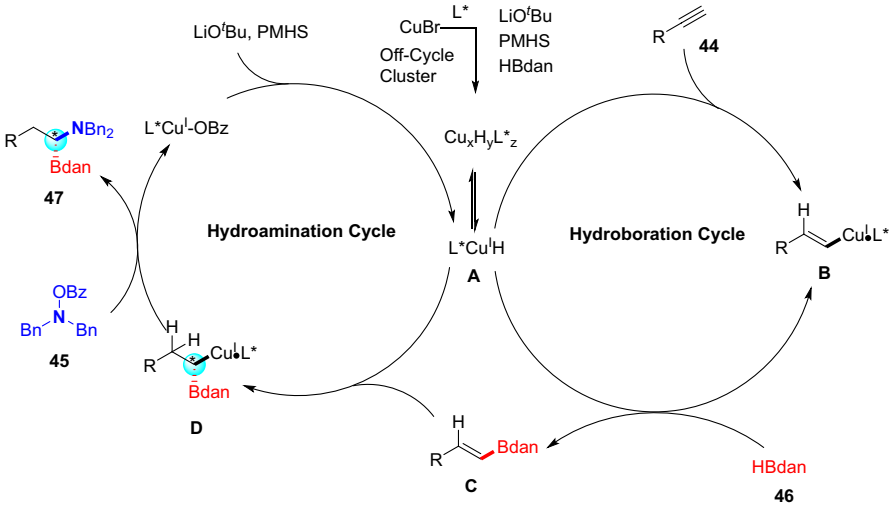
Scheme 19 Plausible reaction pathway for Miura's aminoboration protocol

by-products with high regio-, enatio- and chemoselectivity (Scheme 20). This enantioselective reductive 1,1-difunctionalization will be applicable to a wide range of transformations, allowing alkynes to act as direct progenitors of chiral scaffolds of diverse interest.

The key benefit of this reaction is that it has high enantioselectivity, which prompted the author to investigate the reaction mechanism (Scheme 21). Depending on the order



Scheme 20 Cu(I)-catalyzed aminoboration of terminal alkynes

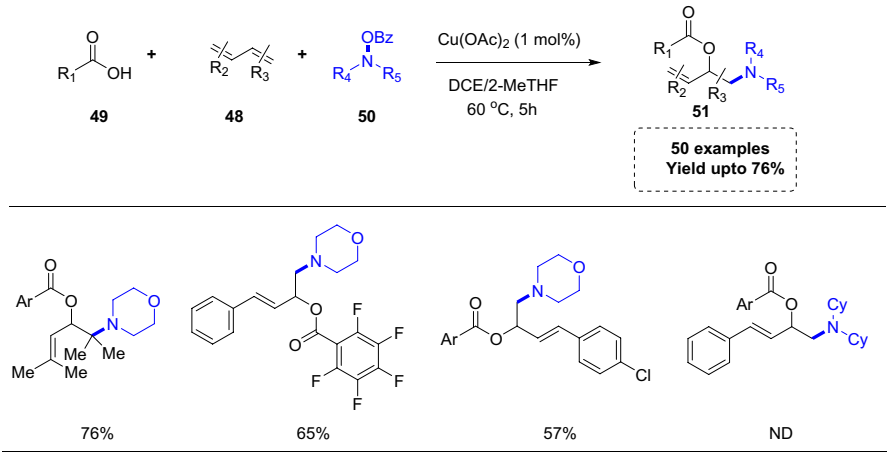


Scheme 21 Proposed reaction pathway for Cu(I)-catalyzed aminoboration

of events, the reaction could be possible through two reaction cycles. In Path A, hydroboration occurs first, while in Path B hydroamination is the first sequence, respectively. Then they put each of the potential intermediates, alkenyl Bdan (**A**) (Path A) and substituted enamine (**B**) (Path B), through the standard reaction conditions to determine which path was operative. Based on the results of this experiment, it was discovered that alkenyl Bdan (**A**) could be transformed into the desired product with enantiomeric excess, similar to the cascade process, whereas enamine (**B**) resulted in decomposition. Additionally, the kinetic studies concluded that path (**A**) was operative.

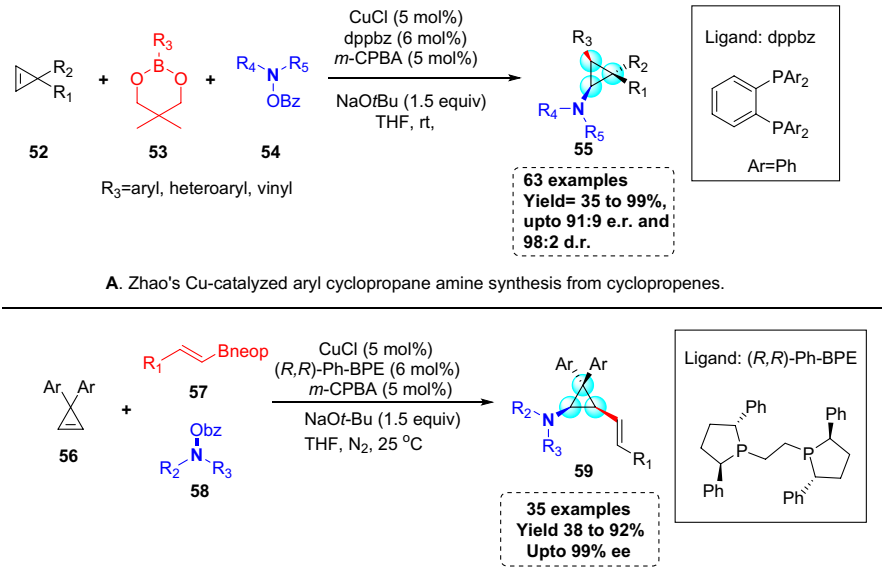
2.1.3 Carboamination

2.1.3.1 Cu Catalyst Wang et al. developed a three-component reaction for the selective functionalization of 1,2 dienes (**48**) using *O*-benzoyl hydroxylamines (**50**) as an

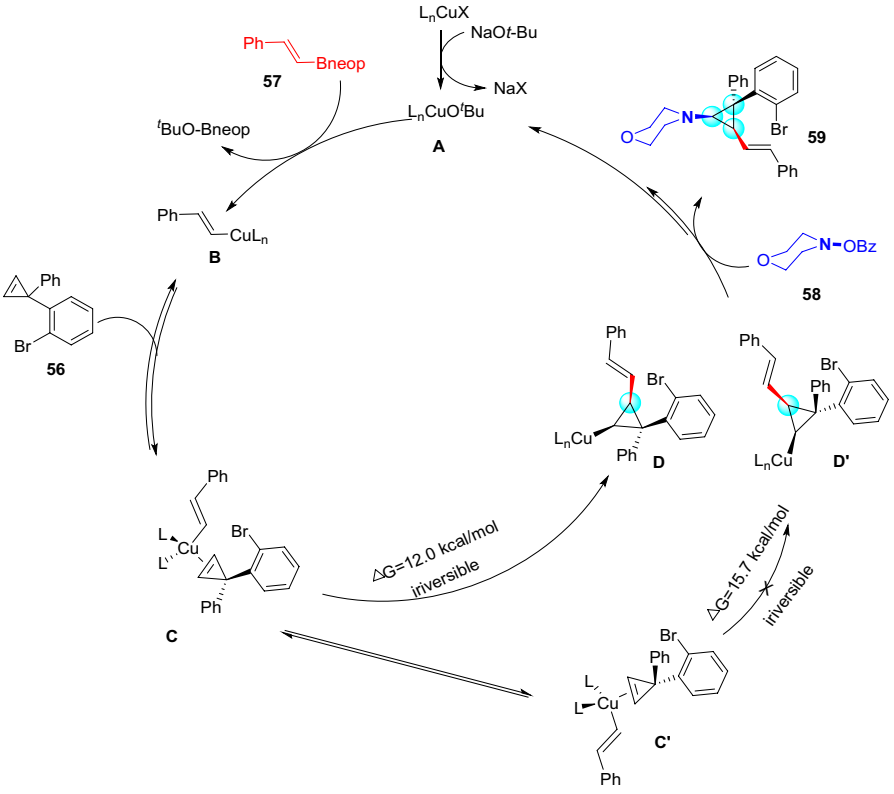


Scheme 22 Cu-catalyzed 1,2 amino oxygenations of 1,3 dienes

electrophilic amination agent, the carboxylic acid (**49**) as a nucleophile in presence of Cu catalyst [61]. This transformation is operative for both terminal as well as internal alkenes and delivers respective amino alcohols (**51**) via amino oxygenation reaction (Scheme 22). After a series of optimization studies and control experiments, the authors concluded that the reaction could be initiated by the Cu-catalyzed elec-



Scheme 23 Zhao's Cu-mediated alkenylamination of cyclopropenes strategy

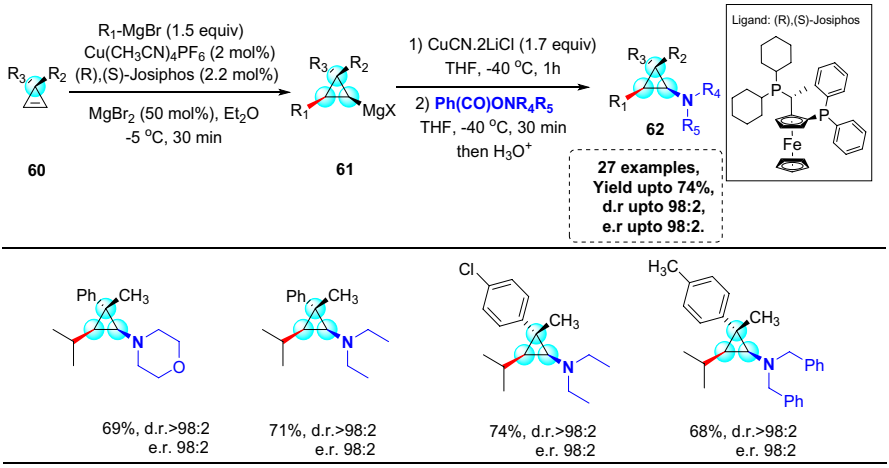


Scheme 24 Proposed catalytic cycle for Zhao's alkenylamination

trophilic amination of diene followed by the oxidative addition of carboxylic acid. The control experiment with BHT radical scavenger indicated that the reaction could proceed through the SET radical pathway.

In 2019, Zhao et al. [62] developed a Cu-mediated multicomponent, 2-arycyclopropyl amine (**55**) synthetic protocol from cyclopropene (**52**) with higher enantioselectivity (Scheme 23A). This was the first general synthetic route for the construction of 2-arycyclopropyl amine (**55**) via intramolecular olefin carbocupration with organo Cu promoted by organoboron reagents through transmetalation. Notably, the biphosphine ligand with a small bite angle is crucial to achieving enantioselectivity. Due to the electronic requirement for migratory insertion, the organoboron reagent with an electron-withdrawing group or electron-deficient species afforded maximum yield as compared to electron-rich species. On the other hand, the electrical character of *meta*- and *para*-substituted cyclopropenes, did not affect the yield of the reaction.

In the following year, the same group came up with a similar strategy with improved enantioselectivity by incorporating selective ligand along with Cu catalyst and alkenyl organoboron reagent. To achieve improved enantioselectivity



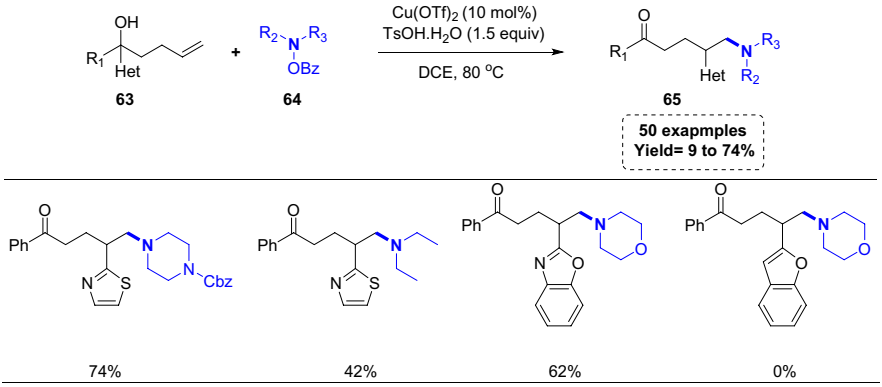
Scheme 25 Marek's Cu-catalyzed asymmetric synthesis of cyclopropylamines

with good-to-excellent yield, the authors examined a series of ligands and observed that the (R, R)-Ph-BPE ligand afforded the desired products in moderate to high yields (38–92%) with up to 99% enantiomeric excess. The variously substituted cyclopropenes (**56**), alkenyl organoboronates (**57**), and *O*-benzoyl hydroxylamines (**58**) successfully participated in this reaction and delivered the corresponding enantiomeric product (**59**) (Scheme 23B) [63].

Scheme 24 presents the proposed mechanism. The CuO*t*-Bu (**A**) is formed in situ by a reaction of Cu species with base NaO*t*-Bu undergoes transmetalation with alkenyl boronates (**57**) to give intermediate (**B**), subsequent migratory insertion with cyclopropene (**56**) to form (**D**) via π-complex (**C**). At step (**C**), the other diastereomeric (**C′**) complex could form because of a larger alkenyl substituent, which occurs in higher-energy intermediate in rapid equilibrium. However, due to the low energy of complex (**C**), it preferentially provides kinetic isomer (**D**) by undergoing faster and irreversible migratory insertion than kinetic isomer (**D′**). Finally, complex (**D**) reacts with the electrophilic aminating agent (**58**) to afford the final product (**59**).

An asymmetric Cu-catalyzed carbometallation of polysubstituted cyclopropenes (**60**) followed by electrophilic oxidation and amination provided rapid access for the synthesis of diastereo- and enantioselective cyclopropanol and cyclopropylamine derivatives (**62**) was described by Marek et al. [64]. The reaction proceeds in two steps, the first step is transmetalation of cyclopropene followed by subsequent electrophilic amination via transmetalation (Scheme 25). The key feature of this reaction is broad substrate scope, good functional group tolerance, retention in configuration, and moderate-to-good yields with high diasteroeo- and regioselectivity.

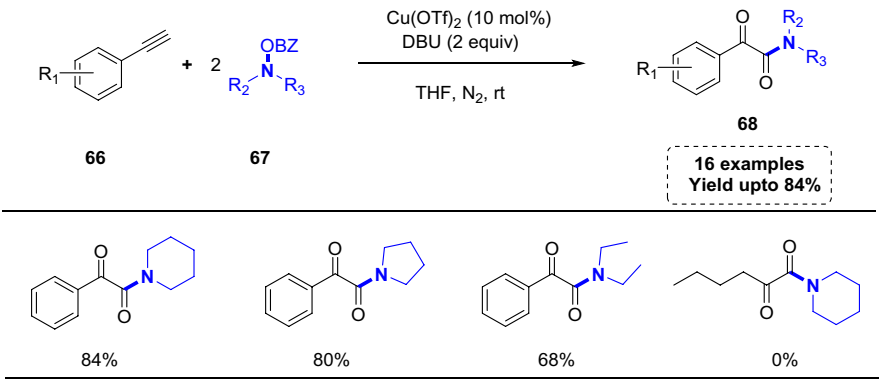
In 2020, Wang et al. disclosed the aminoacyanation of terminal alkene via 1,4 or 1,5-cyano migration using *O*-benzoyl hydroxylamine and *p*-toluene sulfonic acid as an additive under Cu-catalyzed conditions [65]. Although the role of Brønsted acid as an additive for increasing the yield was unclear, it may protonate amines and prevent Cu catalyst deactivation. The experimental studies and



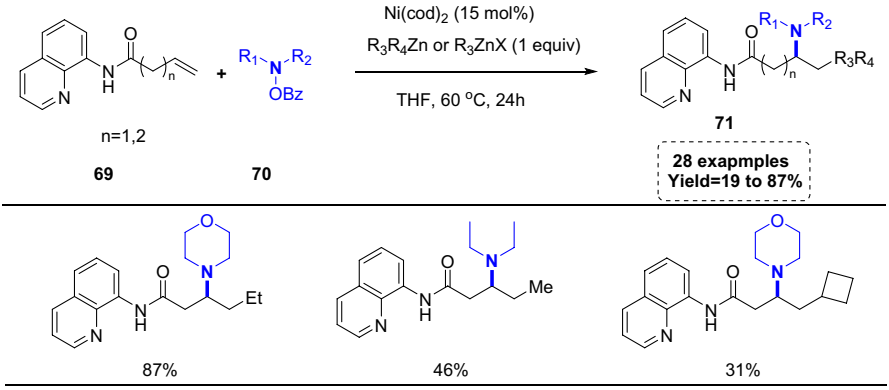
Scheme 26 Wang's Cu(II)-catalyzed distal heteroaryl migration strategy for the synthesis of hetero-arylethylamine derivatives

mechanistic pathway suggested that the reaction could be initiated by Cu-catalyzed amine radical addition to olefin.

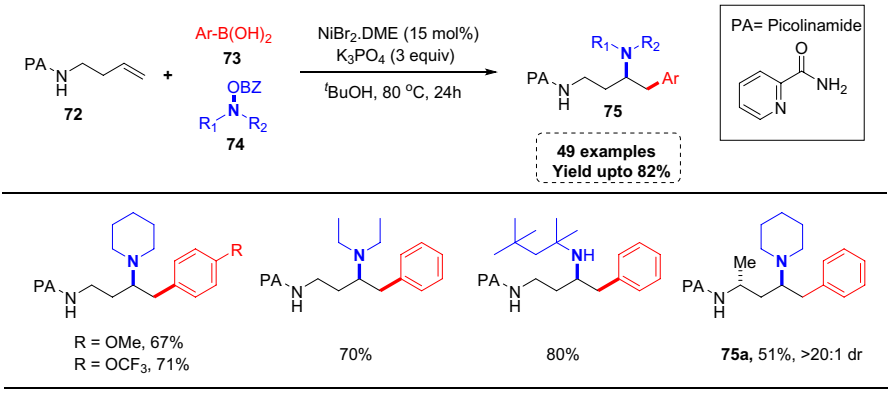
In continuation of the work on radical-based functional group transformation, Wang's group [66] established a new and simple method for synthesizing heteroaryl ethylamine derivatives (**65**) from unactivated alkenes (**63**) by electrophilic amination using *O*-benzoyl hydroxylamine (**64**) followed by distal heteroaryl migration (Scheme 26). The attractive advantage of this transformation is, that it has the appealing feature of removing a barrier for hydroxyl moiety requirement in the field of functional group transformation and applies to a wide range of functionalities, including alcohols, amides, and ether-containing alkenes. Additionally, this protocol could be useful to access the medium-sized ring via the ring expansion process, especially for ketone-bearing hetero arene groups.



Scheme 27 Shen's Cu(II)-catalyzed oxidative amidation of alkynes using *O*-benzoyl hydroxylamine



Scheme 28 Engle's Ni-catalyzed method to afford β- and γ-amino acid or ester derivatives



Scheme 29 Wang's intramolecular *syn* 1,2 arylamination of unactivated aliphatic alkenes

Shen et al. [67] reported a novel and convenient Cu $(OTf)_2$-catalyzed oxidative amidation of terminal alkynes (**66**) for the synthesis of α-α-ketoamides (**68**) by using *O*-benzoyl hydroxylamines (**67**) as aminating reagent as well as oxidant, DBU as a base, in THF at room temperature. This novel synthetic route displayed functional group tolerance and provided α-ketoamides in modest to good yields, However, the aliphatic alkynes and secondary hydroxylamines could not participate in this reaction. This protocol promoted attractive features including the use of easily available *O*-benzoylhydroxylamine as an oxidant as well as aminating reagent (Scheme 27).

2.1.3.2 Ni Catalyst In 2018, Nickel-catalyzed synthesis of β- and γ-amino acid or ester derivatives (**71**) from non-conjugated alkenes (**69**), alkyl or aryl zinc nucleophiles, and *O*-benzoyl hydroxylamine (**70**) electrophiles via intramolecular umpolung carboamination reaction was developed by Engle et al. [68] (Scheme 28). In this transformation, 8-amino quinoline was used as a directing group, which plays

an important role in regiochemical product formation by controlling two-component coupling between N–O electrophiles and zinc nucleophiles. The reaction is compatible with a wide range of functional groups. However, sterically hindered, and primary amines could not afford the corresponding product. Furthermore, the reaction was performed on a gram scale to demonstrate its synthetic utility and delivered the corresponding product with an 83% yield.

In 2021, Wang's group [69] described Ni (II)-catalyzed, picolinamide-directed intramolecular *syn* 1,2 arylamination of unactivated aliphatic alkenes (**72**) utilizing aryl boronic acids (**73**) and *O*-benzoylhydroxylamine (**74**) electrophile (Scheme 29). The control experiments and mechanistic study revealed that bidentate picolinamide helps the formation of 4-, 5-, or 6-membered nickelacyles and enabled the difunctionalization of an alkene by incorporating the aryl group and amino group across the C=C bond. Notably, this transformation delivered a *trans*-isomeric product (**75a**) with great diastereoselectivity in the case of α-substituted alkene, even though two stereocenters were remote from each other.

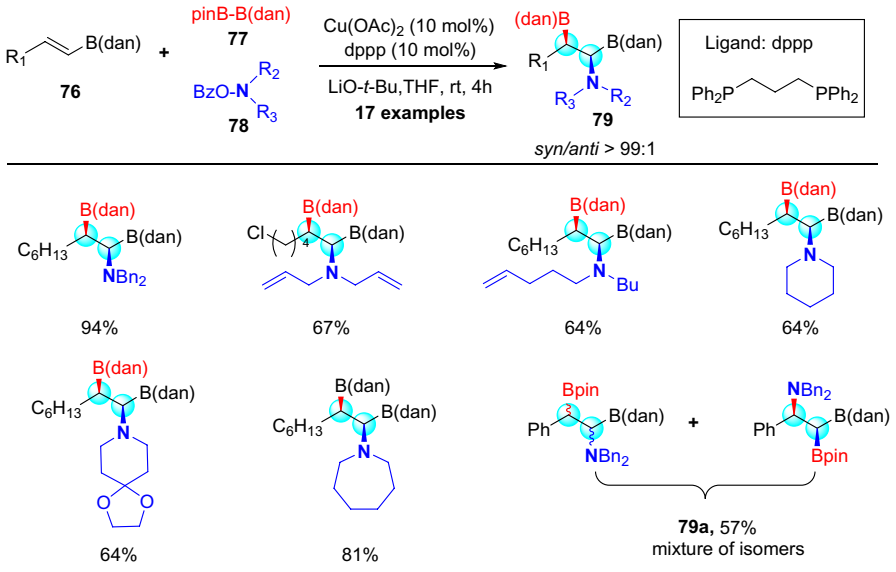
2.2 Amination of Organometallic Nucleophiles

Several synthetic protocols or methods have been developed in which hydroxylamine derivatives are employed in cross-coupling reactions instead of external oxidants (air or O_2). Thus, the transition metal-catalyzed amination of various organometallic reagents gained attention. Several organometallic species have been utilized in recent years, although organoboron derivatives have remained the most preferred reagents.

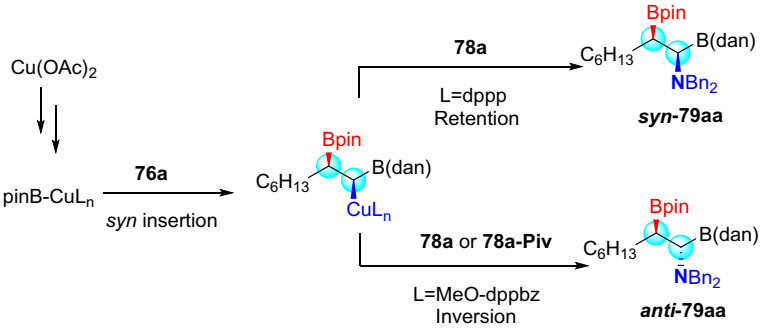
2.2.1 Organoboron Nucleophile

2.2.1.1 Cu Catalyst The amination of organoboron reagents using hydroxylamine-*O*-sulfonic acid was first reported by Brown [70–72], however, the uncatalyzed reaction could only be used to form primary amines. Later, in 2012, Hirano and Miura's group reported the first transition metal-catalyzed aminoboration of organoboron reagents via an electrophilic amination strategy using *O*-benzoyl hydroxylamine as an aminating agent [73]. Later, the same group [54, 55] and others [74–77], disclosed advanced methodologies with increased yield and chemo- and regioselectivity.

In 2016, Miura et al. [78] developed the aminoboration of alkenyl dan boronates (**76**) with diboron reagents (**77**) and *O*-benzoylhydroxylamines (**78**), using $Cu(OAc)_2$ (10 mol%) and dppp ligand (10 mol%) in presence of LiO-*t*Bu base in THF at room temperature (Scheme 30). This reaction provided desired stereoselective *β*-boryl-*α*-aminoboronates (**79**) in good yields (57–92%) in 4 h. A series of sterically demanding substrates such as benzyl, isopropyl, cyclohexyl were compatible under these reaction conditions. However, styrylboronate substrates delivered a mixture of regio and stereoisomers (**79a**) with standard conditions



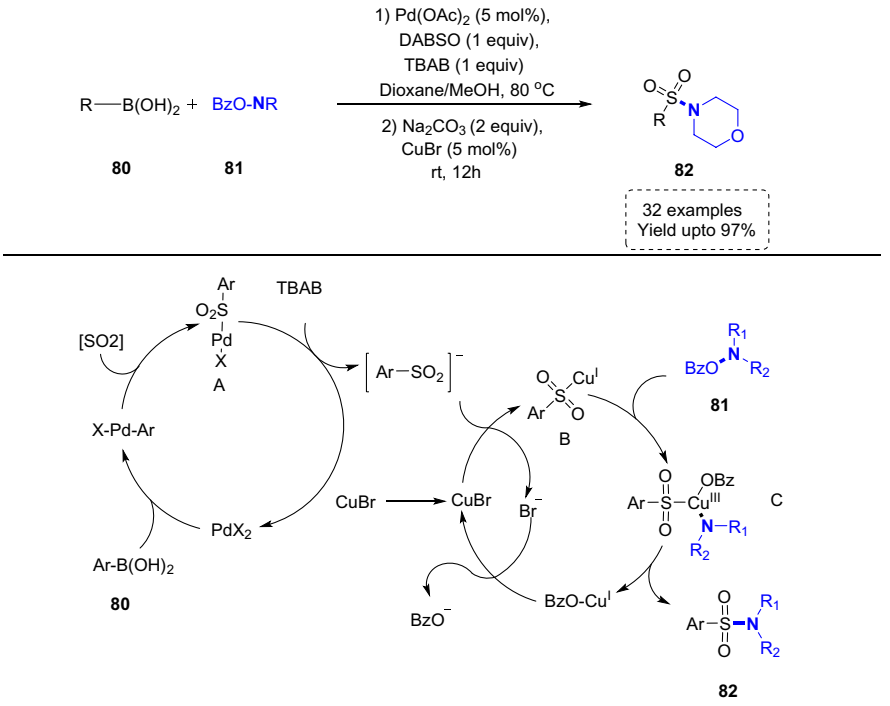
Scheme 30 Cu(II)-catalyzed aminoboration strategy to transform alkenyl dan boronates into *β*-boryl-*α*-aminoboronates



Scheme 31 Possible reaction mechanism for aminoboration of alkenyl dan boronates

(Scheme 30). It is worth mentioning that the application of asymmetric catalysis was achieved by using chiral biphosphine ligands [(R,R)-Ph-BPE].

Although the detailed mechanistic pathway was unclear, based on previous literature a preliminary reaction mechanism was proposed in Scheme 31. Based on the mechanistic studies, they predicted that the stereochemistry of the product (**79aa**) could be determined at the C–N bond-forming step and could be dependent on the external ligand. Further, the hyperconjugation between Cu-C sigma bond and vacant *p* orbital of boron could control the subsequent regioselective *syn*-borylcupration.

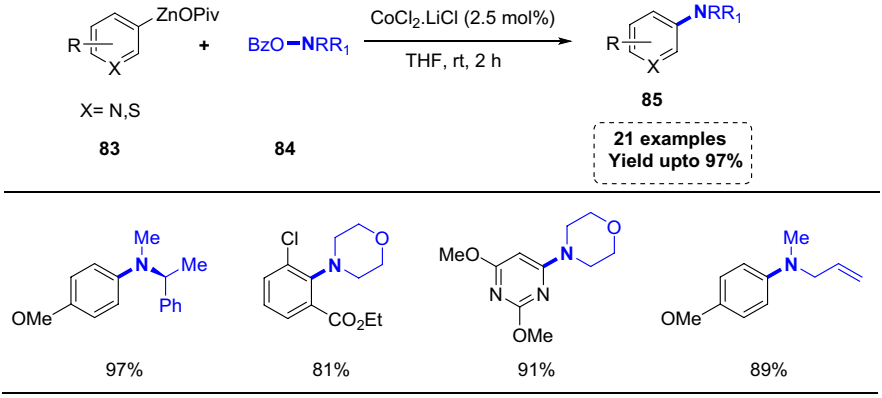


Scheme 32 Tu's one-pot bimetal-catalyzed amino sulfonylation of aryl boronic acid and proposed reaction mechanism

2.2.1.2 Pd Catalyst Tu group [79] described the one-pot synthesis of sulfonamides (**82**) in excellent yields from readily available boronic acids (**80**), DABSO**,** and *O*-benzoyl hydroxylamine (**81**) using Pd–Cu bimetallic catalytic system in the following year (Scheme 32). Good-to-excellent yields (54–97%) were obtained with a variety of functionalized compounds. Based on the mechanistic study, the reaction could proceed through the radical pathway. The proposed reaction mechanism is shown in Scheme 32. Initially, the addition of aryl boronic acid (**80**) on Pd(II), followed by transmetalation and SO_2 insertion gives Pd (II) species (**A**). The sulfinylation catalytic cycle was restored in presence of TBAB resulting in the formation of ammonium sulfinate, followed by sodium carbonate addition to give sodium sulfinate. CuBr was made from $CuBr_2$ and sodium sulfinate through a free radical approach. Then, Cu(I) species (**B**) was formed by a reaction between CuBr and sodium sulfinate in the second transmetalation process. Subsequent oxidative addition with *O*-benzoylhydroxylamine (**81**) generates Cu(III) species (**C**), and further reductive elimination delivers desired product (**82**) and regenerates the catalyst.

2.2.2 Organozinc Nucleophiles

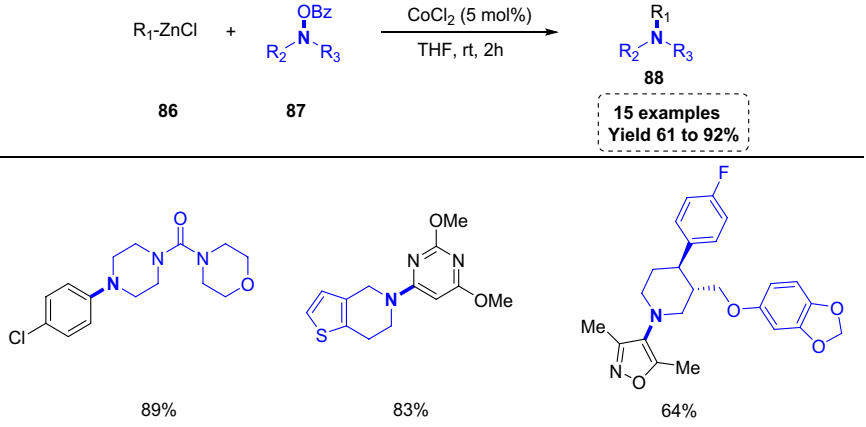
2.2.2.1 Co Catalyst The electrophilic amination using aryl or heteroaryl zinc pivalates (**83**) with *O*-benzylhydroxylamine (**84**) in presence of Co catalyst has been



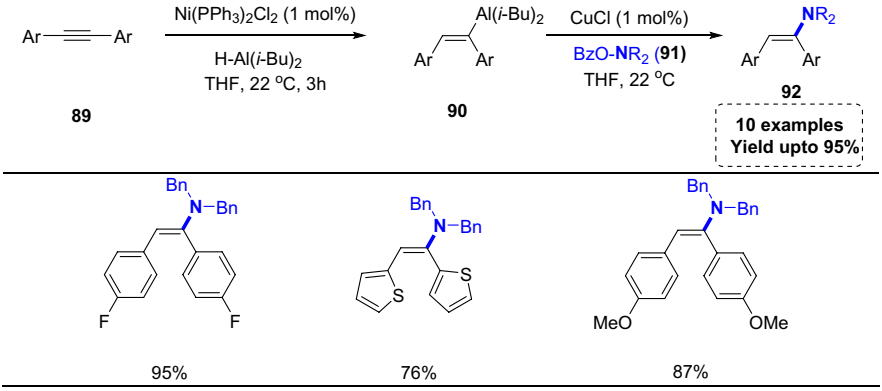
Scheme 33 Cobalt-catalyzed electrophilic amination of organozinc pivalates

developed by Knochel et al. [80], forming a series of corresponding tertiary arylated and hetero arylated amines (**85**) at room temperature (Scheme 33). The strong coordination of the TMP base with cobalt deactivates the catalyst, hence the organozinc pivalates are synthesized by direct metalation using TMPMgCl.LiCl was not applied to this reaction. However, the addition of 5% TMEDA avoided the deactivation of the catalyst. The synthetic utility of this reaction was explored for the synthesis of potential anti-tubercular agent Q203.

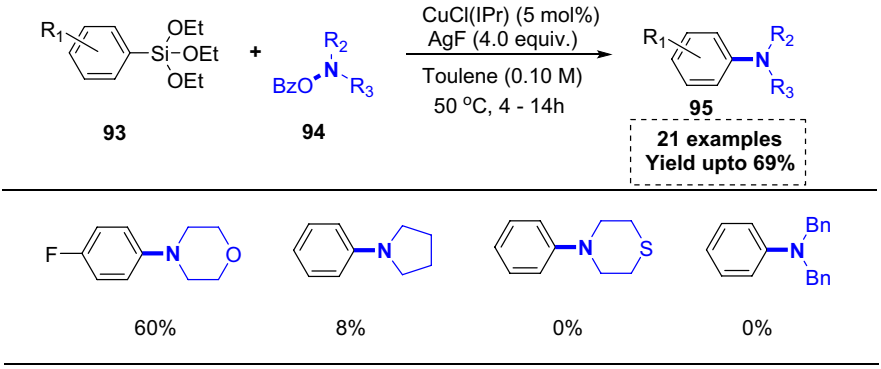
In the following year, the same group described the general method for the synthesis of polyfunctional hydroxylamine benzoates (**87**). These compounds were further used for electrophilic amination of aryl, alkyl, and heteroaryl zinc chlorides (**86**), which delivered corresponding tertiary aminated products (**88**) in the presence of a $CoCl_2$ catalyst. Good functional group compatibility of both aryl zinc chloride and hydroxylamine benzoate was observed in these studies. The synthetic utility of



Scheme 34 Knochel's co-catalyzed electrophilic amination strategy



Scheme 35 Cu(I)-catalyzed electrophilic amination of vinyl aluminum reagents

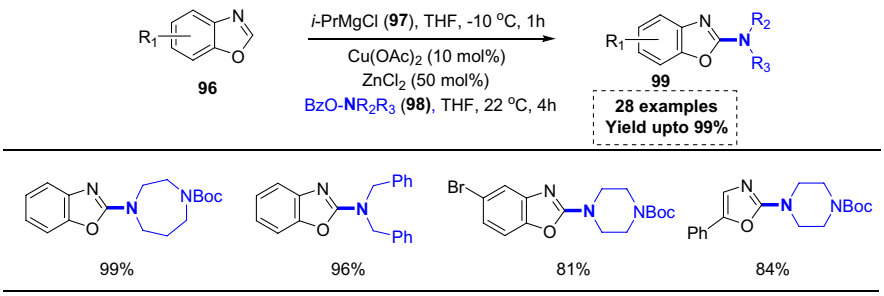


Scheme 36 Cu(I)-catalyzed electrophilic amination of aryl silanes

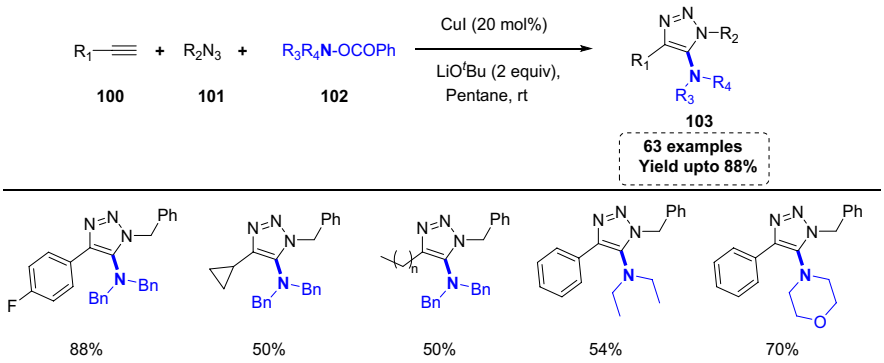
this protocol was proved by the synthesis of complex target amines such as penfluridol and gepirone (Scheme 34) [81].

2.2.3 Organoaluminium Nucleophile

2.2.3.1 Cu Catalyst Cu-catalyzed electrophilic aminations of organometallic reagents with *O*-benzoyl hydroxylamines have emerged as an attractive method for the formation of C–N bonds. In this connection, Yoon et al. [82] investigated a new facile method for the synthesis of 1,2-diaryl-substituted enamines (**92**) via Cu-catalyzed electrophilic amination reaction of *O*-benzoyl hydroxylamines (**91**) with vinyl aluminum reagent (**90**). The reagent (**90**) was formed in situ from the Ni-catalyzed hydroalumination of readily available internal aryl acetylenes (**89**). This method opened a new platform for the preparation of novel diaryl, dialkyl, and heteroaryl substituted enamines with excellent yields and stereoselectivity (Scheme 35).



Scheme 37 Lee's in situ magnesation followed by electrophilic amination of benzoxazole



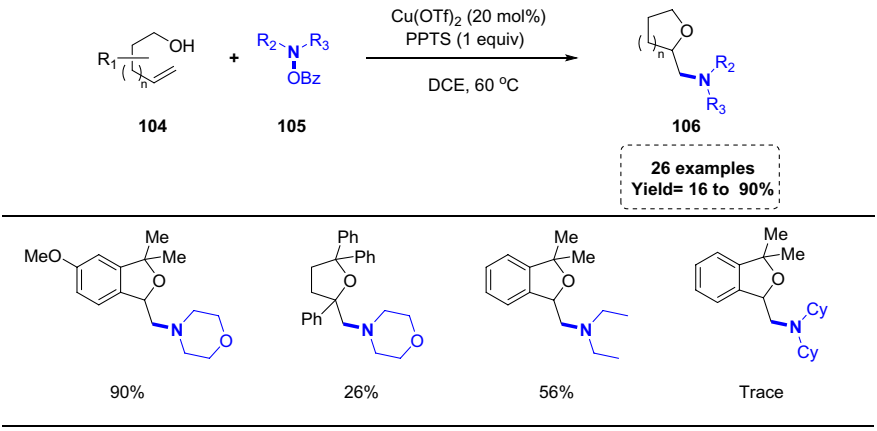
Scheme 38 Cu(I)-catalyzed interrupted click reaction to synthesis of various 5-functionalized triazoles

2.2.4 Organosilane Nucleophiles

2.2.4.1 Cu Catalyst In 2020, Shimokawa et al. [83] reported a Cu-catalyzed electrophilic amination of aryl silanes (**93**) to afford corresponding tertiary anilines (**95**) under mild conditions. In this transformation, silver fluoride plays a crucial role and serves as a base as well as an activator in the catalytic process (Scheme 36). Good-to-moderate yields were obtained with a variety of functionalized compounds.

2.2.5 Organomagnesium Nucleophile

2.2.5.1 Cu Catalyst In 2019, the Lee group [84] demonstrated a one-pot, multicomponent synthesis of 2-amino benzoxazole (**99**) via Cu-catalyzed electrophilic amination. This reaction proceeds through in situ magnesation with *i*-PrMgCl (**97**) followed by electrophilic amination using *O*-benzoyl hydroxylamine (**98**) of benzoxazole derivatives (**96**) to deliver the desired product. The key features of this method are wide substrate scope, functional group compatibility, and milder reaction conditions (Scheme 37).



Scheme 39 Wang's Cu(II)-catalyzed amino etherification of alkenes

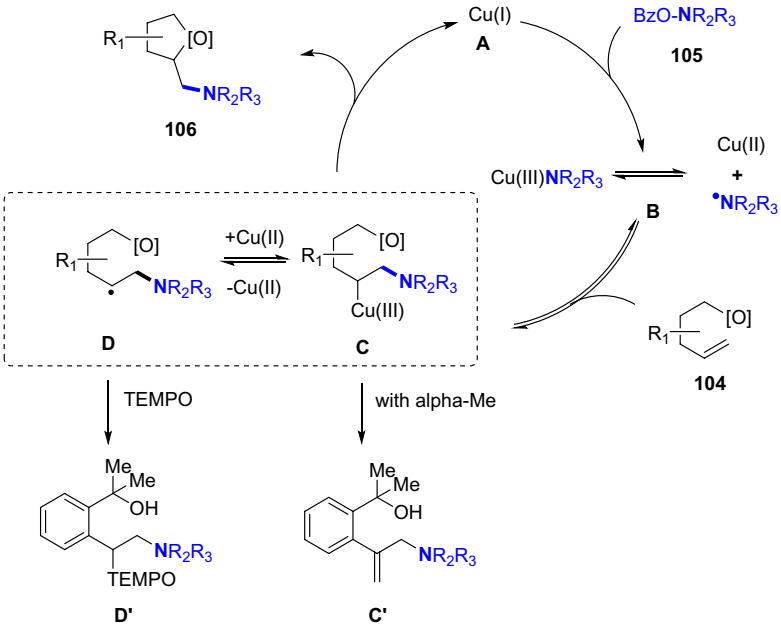
2.3 Annulative Amination

2.3.1 Cu Catalyst

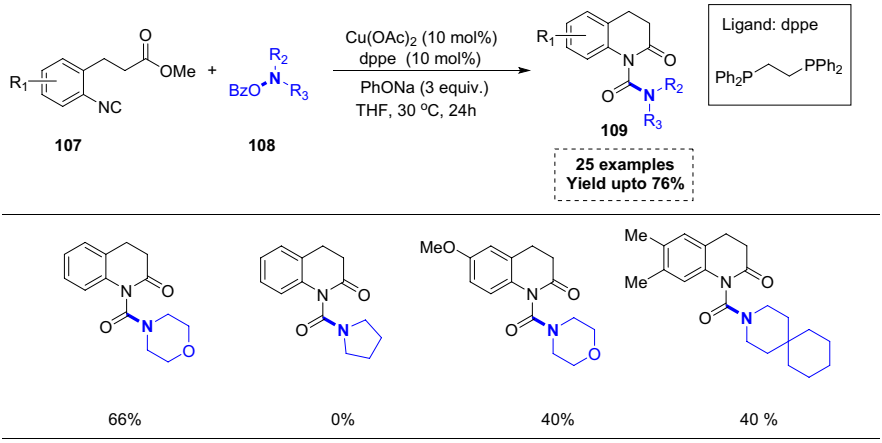
Xu et al. reported [85] Cu(I)-catalyzed interrupted click reaction for the synthesis of various 5-functionalized triazoles (**103**). The proposed reaction proceeds under very mild conditions with the help of a small catalytic amount of inexpensive Cu catalyst without the need for external ligands (Scheme 38). The reaction was also tested for building different-sized rings by intramolecular cyclization. They also demonstrated the two-step synthesis of the antifungal medication thiadiazole. The reaction feature includes a broad substrate scope and good functional group compatibility.

In continuation of their work on Cu-catalyzed electrophilic amination, Wang's group [86] described a novel strategy for the amino etherification of a variety of alkenes (**104**) to afford diverse amino- oxygen-containing cyclized skeletons (**106**). Indeed, the mechanistic investigation revealed that electrophilic amination might trigger the reaction, providing a unique platform for introducing electron-rich amine directly into the alkenes. The key feature of this methodology includes amination with in situ cyclization, broad substrate scope, good functional group tolerance, and good regioselective (Scheme 39).

Based on experimental results, a possible mechanistic pathway was proposed as shown in Scheme 40. The active amino-Cu (III) intermediate (**B**) generated by the reaction of Cu and *O*-benzoylhydroxylamine (**105**), was subsequently triggered by an electrophilic amination of olefins (**104**) to give Cu (III) intermediate (**C**). The intermediate (**C**) leads to the formation of an amino oxygenated product (**106**). Meanwhile, this reactive intermediate (**C**) could undergo β-hydride elimination to deliver allylamine and generate radical species (**D**) via homolytic cleavage, which may be trapped by TEMPO.

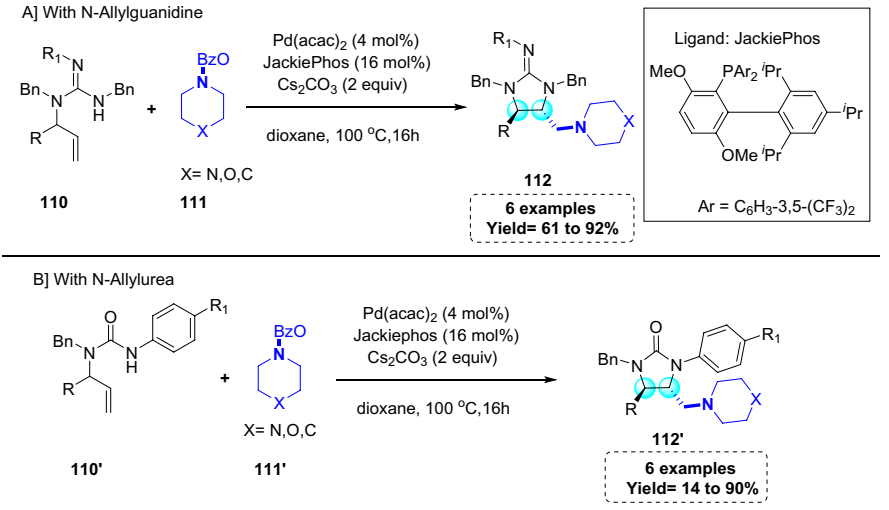


Scheme 40 Plausible reaction mechanism of Cu(II)-catalyzed amino etherification of alkenes

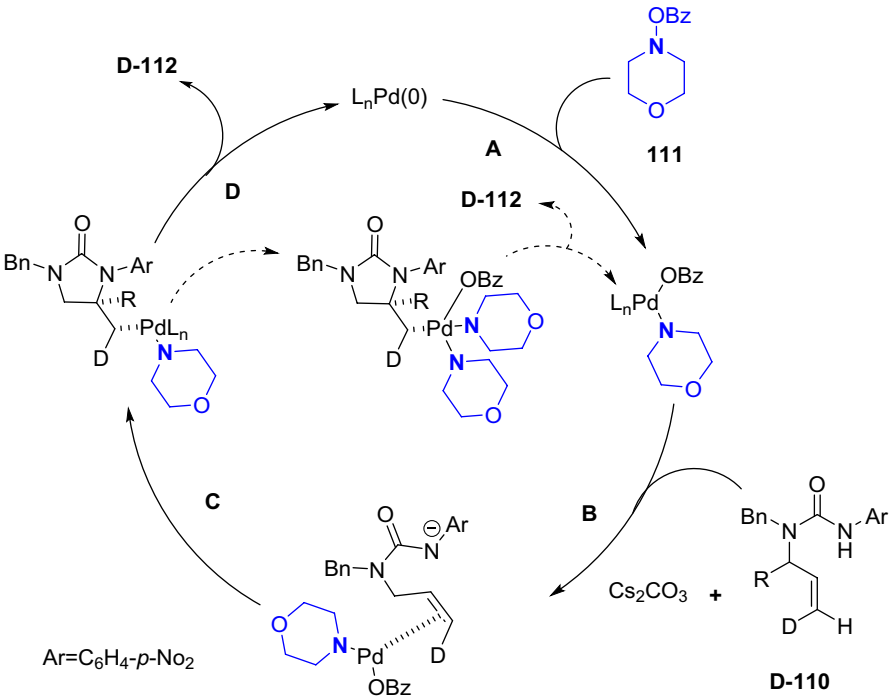


Scheme 41 Wei's annualtive amination of isocyanides

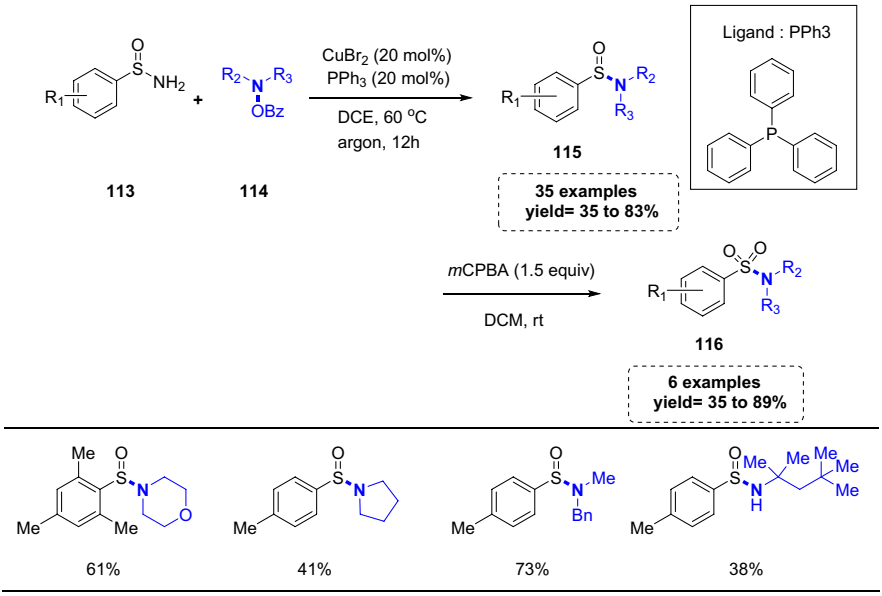
In 2019, Wei et al. [87] described novel and rapid access for the synthesis of dihydroquinolinones (**109**) from readily accessible isocyanides (**107**) and *O*-benzoyl hydroxylamines (**108**) under Cu catalysis. Based on the control experiments and mechanistic studies, they concluded that the reaction might proceed through the isocyanide insertion into the N–O bond, Mumm-type rearrangement, and intramolecular nucleophilic substitution (Scheme 41).



Scheme 42 Wolfe's Pd-catalyzed dialkylamino-methyl group bearing cyclic urea or guanidines derivatives synthesis protocol



Scheme 43 Possible catalytic cycle for Wolfe's amination strategy



Scheme 44 Cu(II)-catalyzed aminosulfonation of *N*-aryl sulfinamides

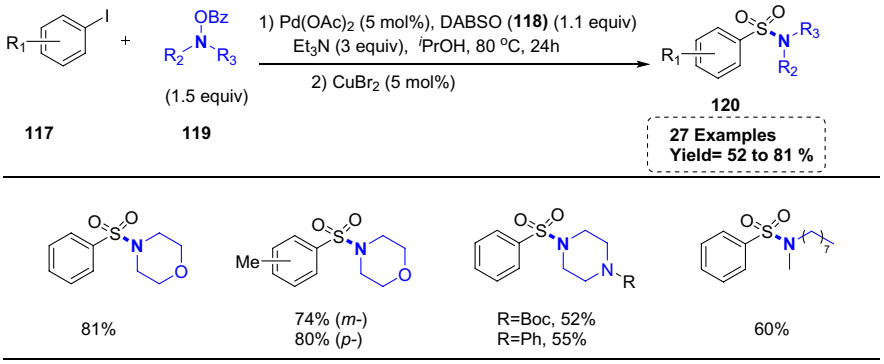
2.3.1.1 Pd Catalyst In 2018, Wolfe et al. [88] disclosed a new and facile strategy for the synthesis of the diastereoselective dialkylamino-methyl group bearing cyclic urea (**112**) or guanidines (**112′**) derivatives from *N*-allylurea (**110**) or *N*-allyguanidines (**110′**) and *O*-benzoyl hydroxylamines (**111**) as electrophilic amination partner via Pd-catalyzed deamination reaction (Scheme 42). Cyclic hydroxylamines performed well under standard conditions. However, acyclic hydroxylamine derivatives especially derived from *N*-methyl benzylamine gave a complex mixture of products. Likewise, the allyl methyl bearing allylguanidines (**110**) and allylurea (**110′**) substrates delivered the *N*-aminated products in good yields with moderate diastereoselectivity (3:1 dr).

The mechanistic pathway indicated that this transformation proceeds through the sp^3C and sp^3N bond formation (Scheme 43), which was facilitated by bulky, electron-deficient JackiePhos ligand. The anti-addition of alkene-bearing *β*-hydrogen atom on amino-Pd complex undergoes sp^3C-sp^3N bond-forming, followed by reductive elimination afforded corresponding cyclic urea or guanidines derivatives.

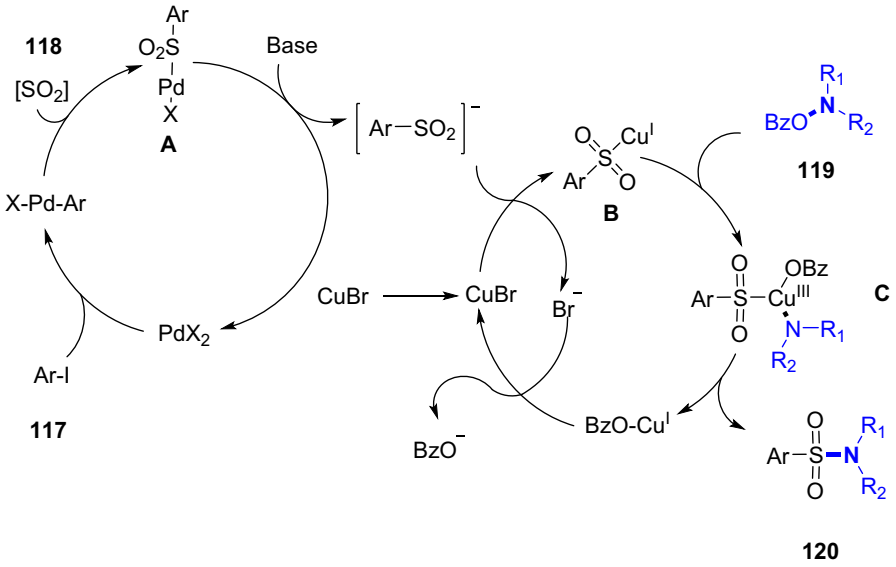
2.4 Aminosulfonation

2.4.1 Cu Catalyst

A novel and convenient cascade strategy to synthesize *N*-aryl sulfonamides (**116**) through Cu(II)-catalyzed transsulfinamidation of sulfinamide with *O*-benzoyl hydroxylamine was explored by Bolm et al. (Scheme 44) [89]. Subsequent oxidation with *m*-CPBA gives corresponding sulfonamides in higher yields (35–89%). The



Scheme 45 Bimetal-mediated aminosulfonylation of aryl iodides

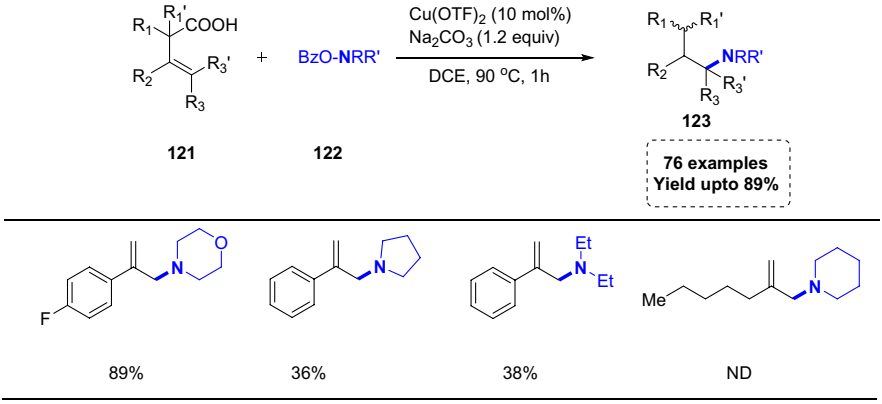


Scheme 46 Plausible reaction mechanism for bimetal-mediated aminsulfonylation

substituents such as halo, cyano, methoxy, carboxyl group, etc., on *N*-aryl sulfinamides exhibited good compatibility even though the steric effect could not alter the reaction outcome. Additionally, reactions with various hydroxylamines were performed well and delivered the product in good-to-excellent yields. On the other hand, increased steric hindrance around the amino group decreases the reaction yield.

2.4.2 Pd Catalyst

In 2017, Le and Tu's group [90] developed a method for direct aminosulfonylation of aryl iodides (**117**) through ligand-free bimetal-mediated one-pot reaction (Scheme 45).



Scheme 47 Wangs's Cu(II)-catalyzed decarboxylative amination of *β, γ*-unsaturated carboxylic acids

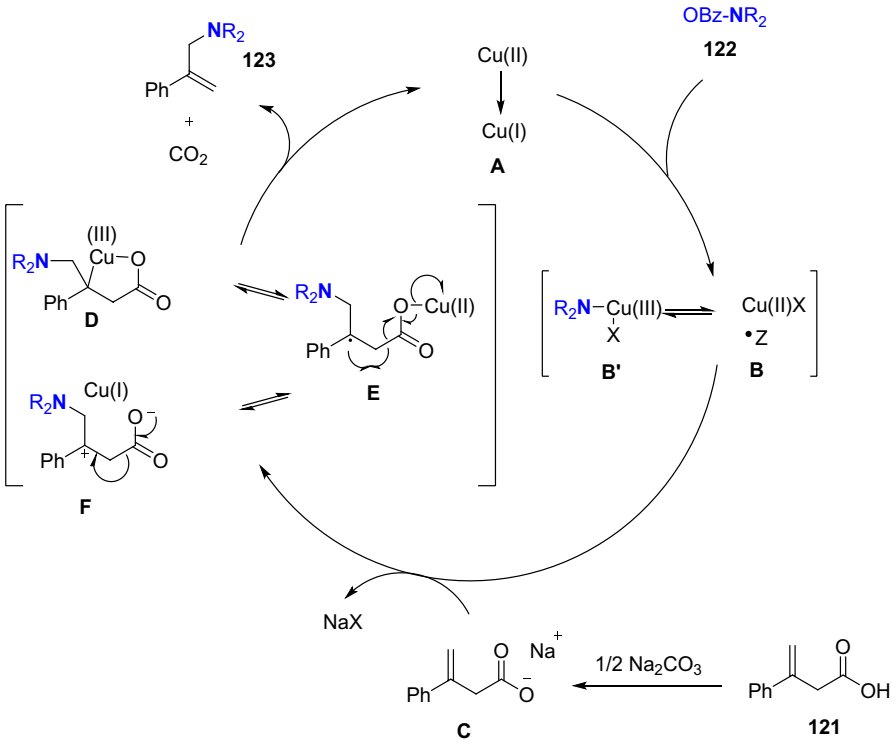
Moderate-to-good yields (52–81%) were obtained with a variety of functionalized compounds. Based on the mechanistic route of this reaction, Cu(I) species could be accountable for the electrophilic amination of sulfinate, which was generated in situ from CuBr. The key features of this transformation are one-pot, ligand-free, broad substrate scope, good functional group transformation, low catalyst loading, and straightforward access to structurally diverse sulfonamides.

A plausible reaction mechanism was proposed as shown in Scheme 46. Initially, the addition of aryl iodide (**117**) on Pd (II), followed by transmetalation and SO_2 (**118**) insertion gave Pd (II) species (**A**). The sulfinylation catalytic cycle was restored in the presence of a base resulting in the formation of ammonium sulfinate, followed by sodium carbonate addition to give sodium sulfinate. CuBr is made from $CuBr_2$ and sodium sulfinate through a free radical approach. Then, Cu(I) species (**B**) was formed by a reaction between CuBr and sodium sulfinate in the second transmetalation process. Subsequent oxidative addition with *O*-benzoylhydroxylamine (**119**) generates Cu(III) species (**C**), and further reductive elimination delivers desired product (**120**) and regenerates the catalyst.

2.5 Decarboxylative Amination

2.5.1 Cu Catalyst

Wang et al. transformed the conjugated *β,γ*-unsaturated carboxylic acids (**121**) into respective allylic amines (**123**) by employing Cu catalyst and *O*-benzoylhydroxylamines (**122**) via decarboxylation (Scheme 47) [91]. Under the standard condition, both electron-donating and -withdrawing groups performed successfully to give corresponding allylic amines in good-to-excellent yields. However, the steric hindrance at the *γ*-position of carboxylic acid, as well as pyrrolidine-based and acyclic hydroxylamines, delivered the desired product in low yields. Notably, the reaction did not proceed in the case of substituted aliphatic

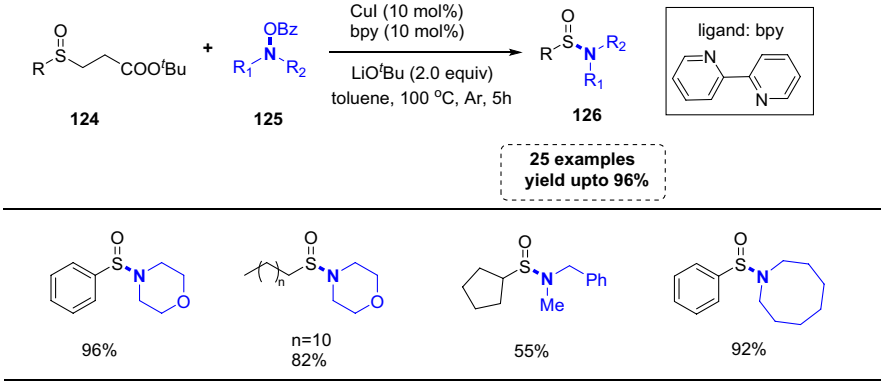


Scheme 48 Proposed reaction pathway for Wang's methodology

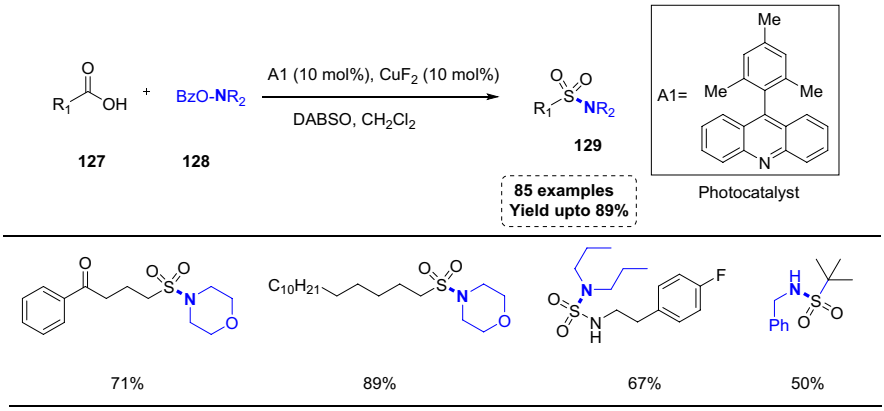
substrates. This reaction is also applicable for decarboxylative alkylation and sulfonylation of *β,γ*-unsaturated carboxylic acids.

The proposed reaction mechanism pathway is displayed in Scheme 48. Firstly, the active Cu(I) catalyst was generated by the deprotonation of Cu (II) complex (**A**) followed by the oxidative addition of radical precursor *O*-benzoylhydroxylamine (**122**) to Cu(I) to give complex (**B**). This could exist in equilibrium with a Cu (III) species (**B'**). Secondly, the intermediate (**D**) and (**F**) were obtained by the following addition to olefins (**E**) that could occur at the *γ*-position of *β, γ*-carboxylic acids (**121**). Finally, the intermediate (**D**) and (**F**) undergo decarboxylation giving the desired product (**123**) with the regeneration of Cu (I).

In 2018, a general one-pot strategy for the construction of diverse sulfonamides (**126**) was developed by Zhang et al. using in situ generated sulfenate anion (**124**) and *O*-benzoyl hydroxylamine (**125**) as an electrophilic aminating agent [92]. After a series of optimization studies, they observed that using 10 mol% of CuI catalyst, 10 mol% of bpy ligand, and 2 equiv. of LiO^tBu base afforded maximum yield (up to 96%) in toluene at 10 °C. Some highlights of this reaction were wide substrate scope, easily available precursors, mild conditions, and good functional group tolerance (Scheme 49).

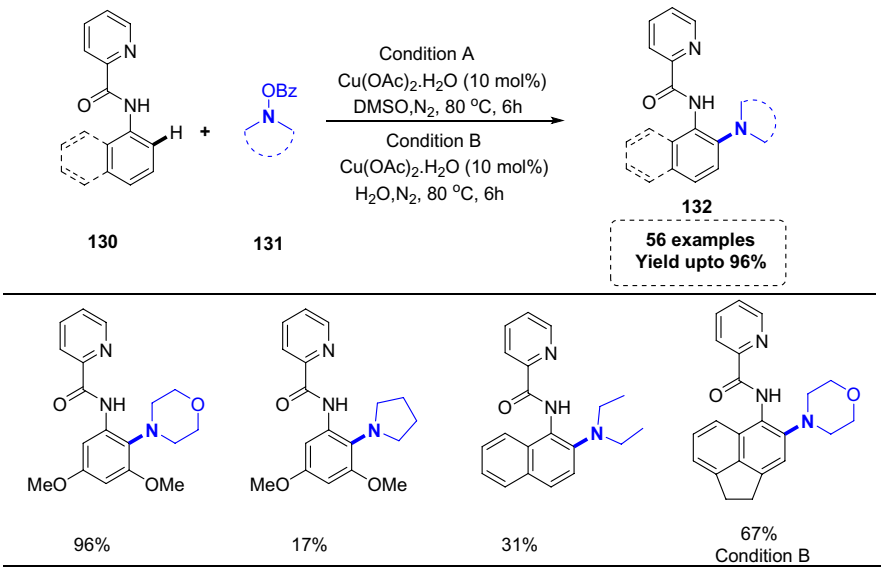


Scheme 49 Zhang's Cu(I)-catalyzed a one-pot amination strategy for the construction of diverse sulfonamides



Scheme 50 Cu-catalyzed decarboxylative amidosulfonation of carboxylic acids

In 2021, the Larionov group [93] described the decarboxylative amido sulfonation strategy for the direct access of sulfonamide (**129**) from carboxylic acid (**127**). The reaction involves the electrophilic and nucleophilic amination of carboxylic acid to sulfonic acid under the dual catalyzed system, i.e., photocatalyst acridine and Cu catalyst in a one-pot fashion. This protocol showed the wide substrate scope for both carboxylic acids and hydroxylamines and good functional group compatibility. Remarkably, not only Cu(I) but also Cu (II) catalysts such as CuF_2 could also promote this transformation (Scheme 50). In the absence of light and photocatalyst, the acridine reaction did not proceed. Other classes of photocatalysts such as Ir and Ru-based failed to deliver the desired sulfonamides. Certainly, the slight modification in standard reaction conditions could promote the amino sulfonation of anilines.



Scheme 51 Jana's Cu(II)-catalyzed selective *ortho* amination of arenes

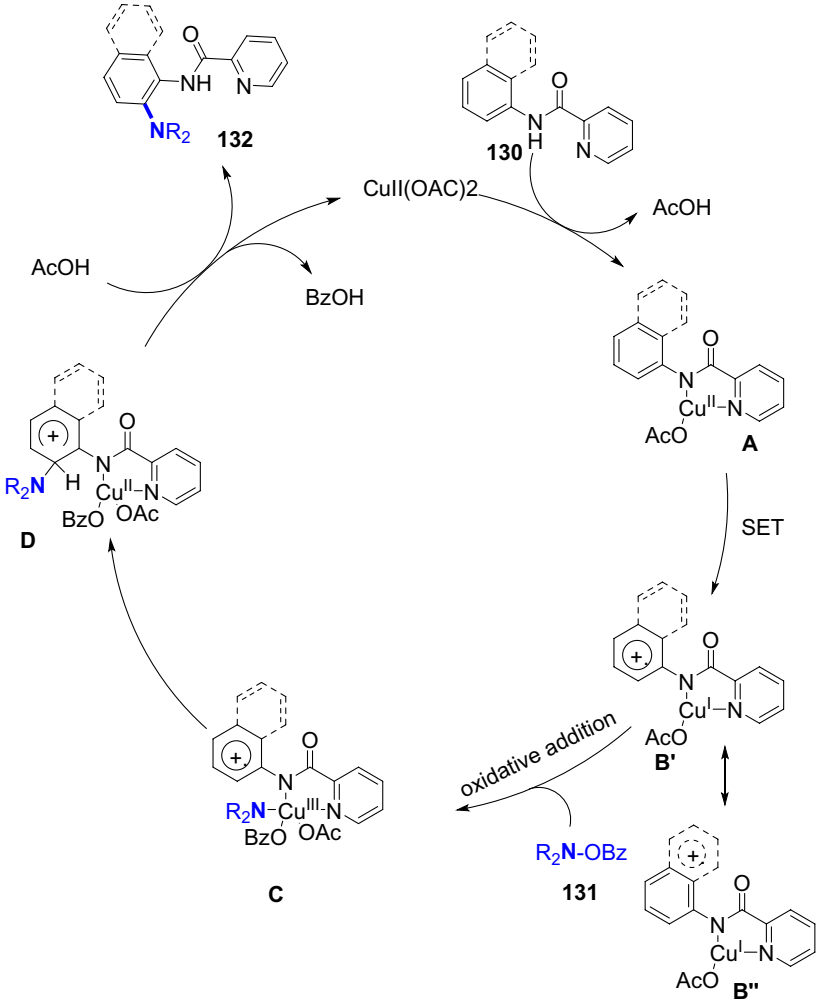
2.6 Ortho Amination

2.6.1 Cu Catalyst

Jana et al. [94] achieved Cu(II)-catalyzed, *ortho*-selective amination by employing *O*-benzoyl hydroxylamines (**131**) as a nitrogen source at 80 °C. The amino group was installed at the *ortho* position of arenes or polycyclic arenes (**130**) involving naphthalene, quinoline, etc., with the assistance of 2-picolinamide as a directing group. This reaction showed a broad range of substrates scope and afforded corresponding anilines, napthylamines, and heterocyclic amines (**132**) in good-to-excellent yields. Both cyclic and acyclic hydroxylamines were well tolerated, however, except for six-membered cyclic amines, other cyclic compounds showed comparatively low yields. Notably, this reaction is air and oxygen-sensitive, in presence of air or oxygen product decomposition or over oxidation may occur, lowering the yields. It is worth noting that this reaction could deliver a corresponding aminated product in H_2O (Scheme 51).

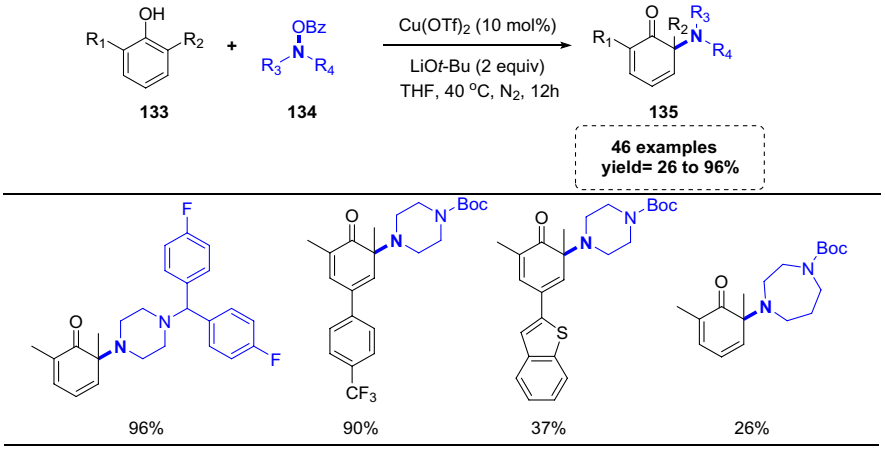
A preliminary mechanistic pathway for Cu(II)-catalyzed amination is shown in Scheme 52. The Cu(II) catalyst coordinated with bidentate 2-picolinamide (**130**) generates Cu-complex (**A**). This intermediate further undergoes single-electron reduction via the SET process to form Cu(I) complex (**B′**), which could be more stable for naphthalene form (**B″**). Subsequent oxidative addition with *O*-benzoyl hydroxylamine (**131**) generates Cu (III) complex (**C**) followed by amine allocation (**D**) deprotonation offers desired aminated product (**132**) with catalyst recyclization.

Guo et al. [95] described an efficient approach that furnishes α-aminocyclohexa-2,4-dienones (**135**) from simple phenols (**133**) and *O*-benzoyl hydroxylamines (**134**)

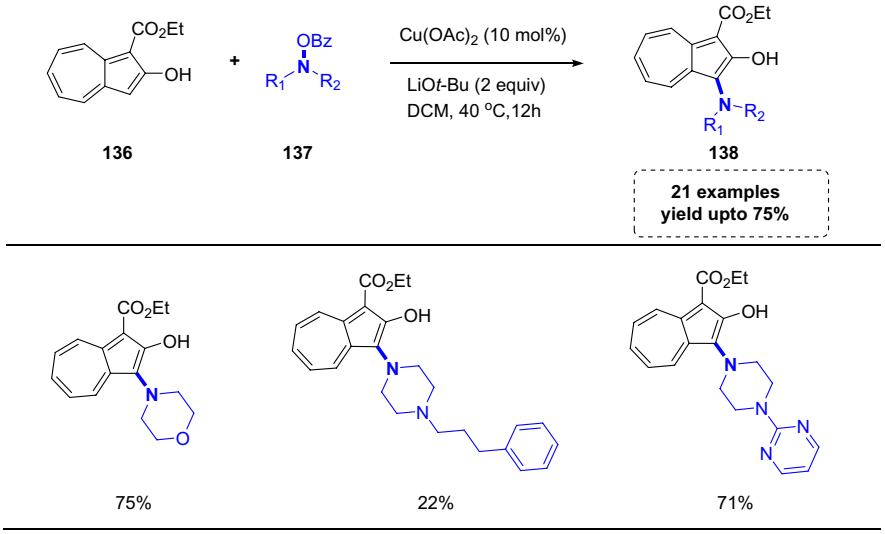


Scheme 52 Possible catalytic cycle for Jana's Cu (II)-catalyzed selective *ortho* amination

with the aid of Cu(II) catalysis (Scheme 53). Based on the optimization studies, 10 mol% of $Cu(OTF)_2$, 2 equiv. of LiO-*t*Bu gave moderate-to-excellent yields (26 to 96%) in THF at 40 °C under a nitrogen atmosphere for 12 h. This transformation showed excellent functional group tolerance and broad substrate scope. Furthermore, when *ortho*- and *para*-substituted phenols were used, the reaction produced selective *ortho*-aminated compounds concerning the hydroxyl group with good yields. Additionally, both cyclic and acyclic *O*-benzoyl hydroxylamines were performed well under the standard conditions. Though the preliminary mechanistic pathway of this transformation is unclear, based on the control experiments and kinetic studies the authors suggested that the reaction could proceed in two possible



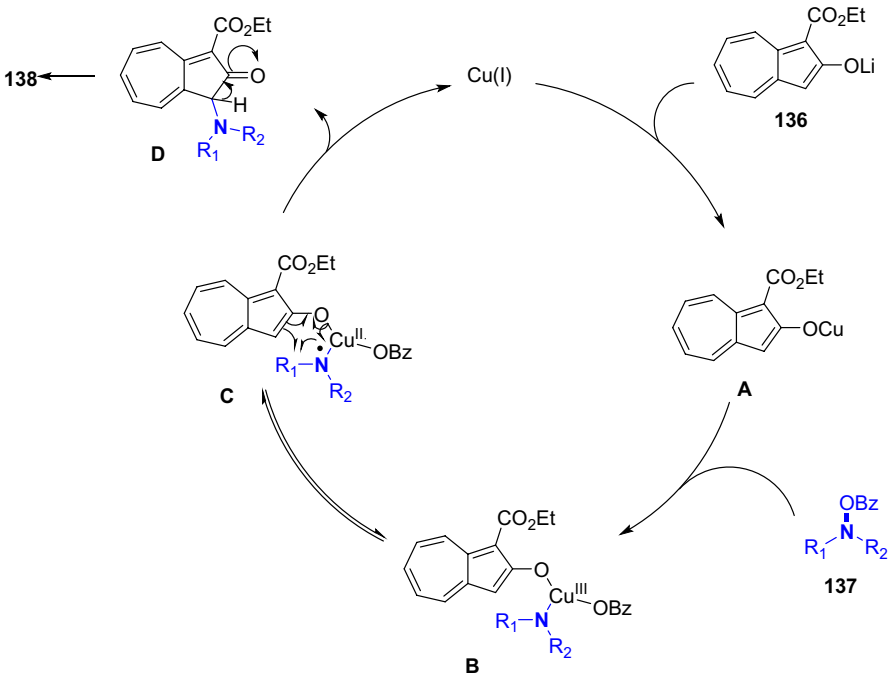
Scheme 53 Guo and Wang's ortho amination of simple phenols



Scheme 54 Guo and Wang's Cu(I)-catalyzed ortho amination of 2-azuenols

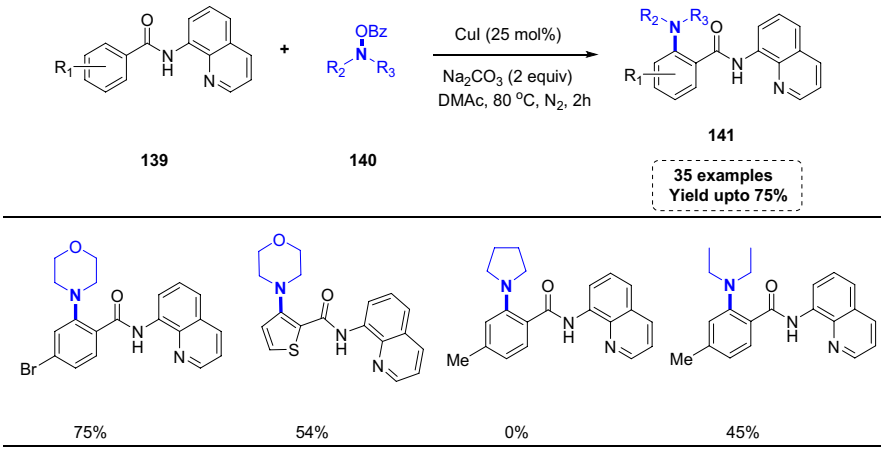
ways. Either by SET with N center radical attack on phenol or through an inner space process involving nucleophilic addition of phenol to an electrophilic Cu (III)-amino complex.

In 2021, the same group disclosed a protocol for the synthesis of selective *ortho*-amino azuenols (**138**) under mild reaction conditions. In this reaction 2-azuenols (**136**) react smoothly with *O*-benzoylhydroxylamines (**137**) under Cu(I) catalyst,

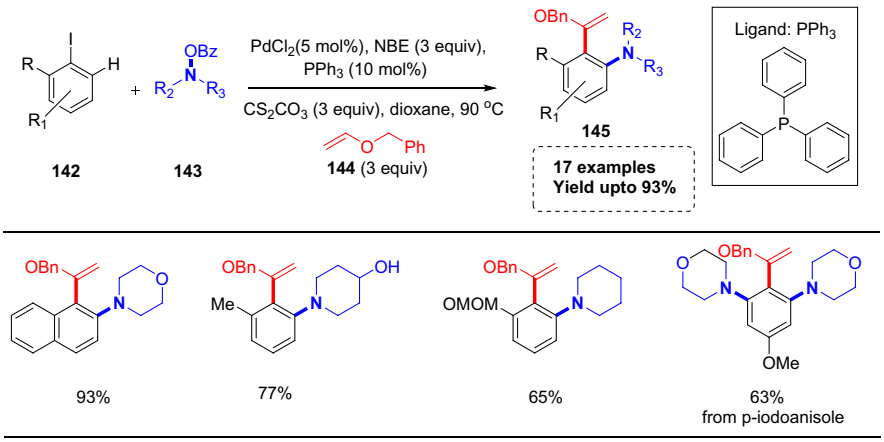


Scheme 55 Proposed reaction pathway for Cu(I)-catalyzed ortho amination of 2-azuenols

10 mol% Cu (OAc), 2 equiv. LiO*t*Bu affording 3-amino azuenlos with moderate-to-good yields (up to 75%) in DCM at 40 °C for 12 h. The mild reaction conditions, a simple approach, good functional group tolerance, and a scalable strategy are the key features of this methodology [96] (Scheme 54). Notably, even when the reaction was carried out in an open atmosphere, the yield was unaffected.



Scheme 56 Cu(I)-catalyzed amination of 8-aminoquinoline tethered benzamides



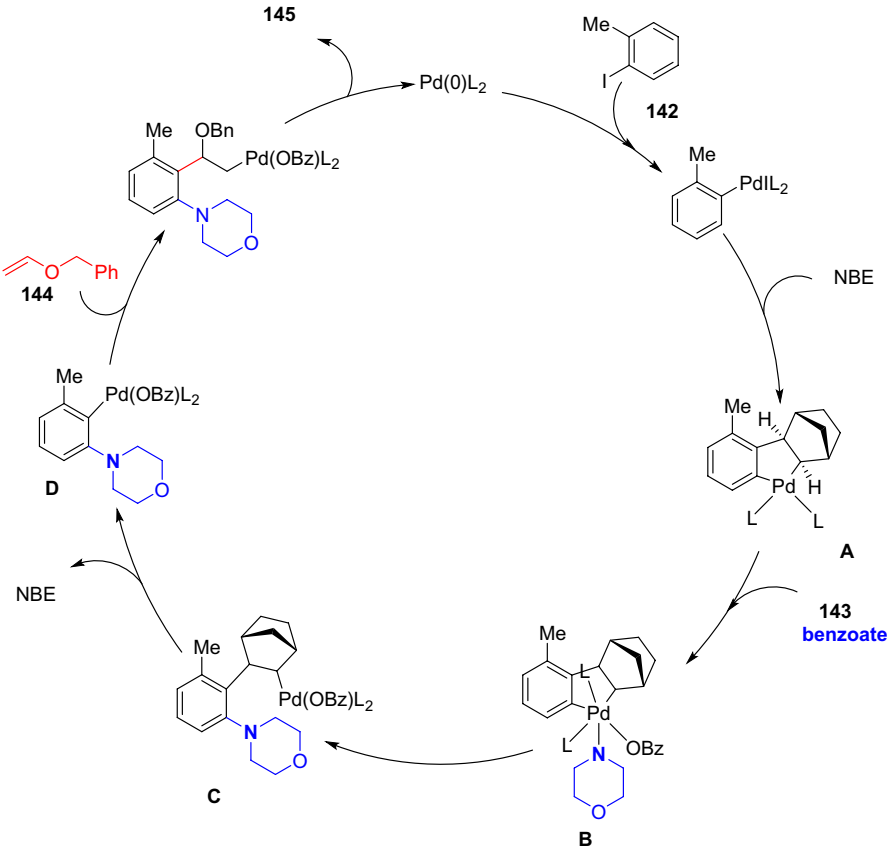
Scheme 57 Wang's Pd/Norbornene promoted *ortho* amination and *ipso* vinyl etherification of aryl iodides

The plausible reaction mechanism (Scheme 55) involves the formation of Cu(I) azulenolate species (**A**) from the ligand exchange of Cu(I) with azulenolate (**136**). Cu (III) species (**B**) is formed by the oxidative addition of *O*-benzoylhydroxylamine (**137**) to Cu(I). The equivalent Cu (II)N-centered radical form (**C**) Cu (II)·NRR′, is formed by the quick equilibration of (**B**). Then, the inner space electron transfer process would generate intermediate (**D**) by the attack of N-centered radical on the *ortho* position of azuenols via the pseudo-five-membered ring and recyclization of Cu (I). Finally, dearomatization of (**D**) offers the final product (**138**).

In 2021, Rao et al. [97] reported a Cu-catalyzed electrophilic amination of benzamides (**139**) to form selective mono-aminated products (**141**) using 8-aminoquinoline as a directing group (Scheme 56). The benzamides with a variety of functional groups underwent the reaction smoothly and delivered the product in good yields. Likewise, diverse hydroxylamines (**140**) performed well, However, the five-membered cyclic pyrrolidine hydroxylamines could not be achieved under this reaction condition. On the other hand, acyclic hydroxylamines participated in this transformation with relatively low yields. Further, the preliminary mechanistic pathway of this reaction was investigated by control experiments with radical scavengers (TEMPO) and competitional experiments of benzamide and *O*-benzoyl hydroxylamines. These results revealed that C–H activation might be preferable in the rate-determining step and that the reaction might not follow the radical pathway.

2.7 Catellani Reaction

The Catellani reaction was discovered by Marta Catellani [98] and is a strong method to synthesize highly substituted aromatic compounds and fused aromatic rings due to its ability to functionalize both *ortho*- and *ipso*-positions of aryl iodides in a single transformation [99–103]. Dong et al. introduced the first Pd/

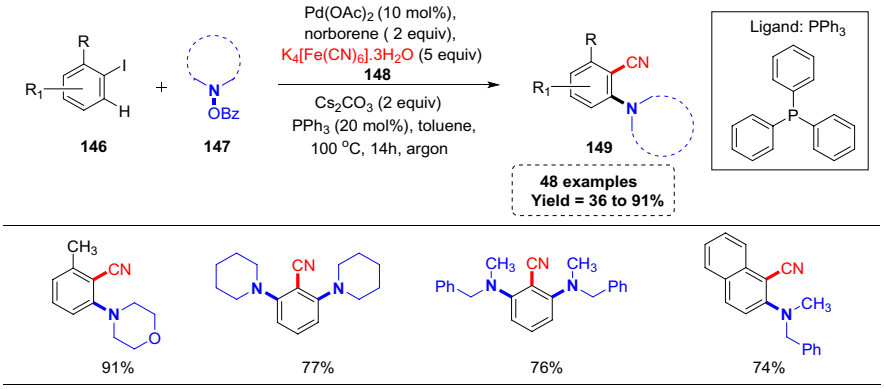


Scheme 58 Proposed catalytic cycle for Wang's *ortho* amination and *ipso* vinyl etherification

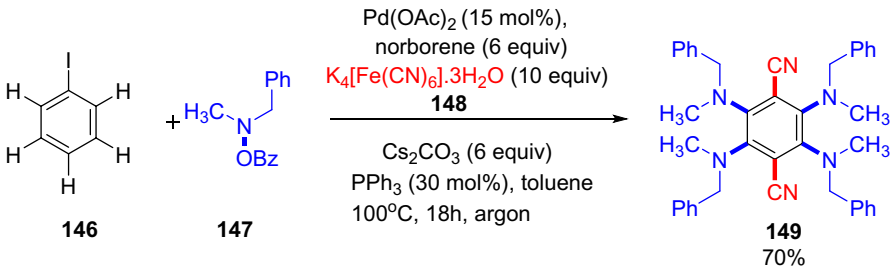
norbornene-catalyzed C–H amination of aryl halides in 2013, incorporating amino group on the *ortho*-position of the halogen substituent [104]. Later, Chen group [105, 106], and others [107–110] reported novel and modified synthetical protocols with broad substrate scope and high selectivity. In this section, we are discussing recent breakthroughs made in Catellani C–H amination.

In 2016, Wang et al. [111] demonstrated a Pd/norbornene-catalyzed selective *ortho* amination of iodoarenes (**142**) using *O*-benzoyl hydroxylamine electrophile (**143**) via Catellani-type reaction. The *ortho* electrophilic amination followed by *ipso* vinyl ether termination delivered the corresponding diverse *ortho* aminated *O*-acetyl aniline derivatives (**145**) in moderate-to-excellent yields (44–94%). The series of control experiments and mechanism studies suggested that the benzyl vinyl ethers could serve as an alternative for carbonyl sources in Pd/norbornene catalysis for final termination reaction to deliver the desired product with selectivity (Scheme 57).

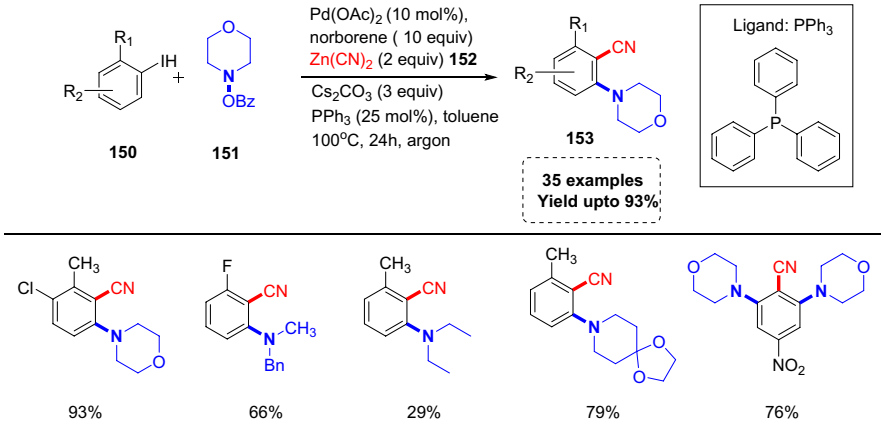
The mechanistic hypothesis of Pd/norbornene-catalyzed *ortho* amination reaction is illustrated in Scheme 58. Primarily, the aryl Pd (II) species gives the



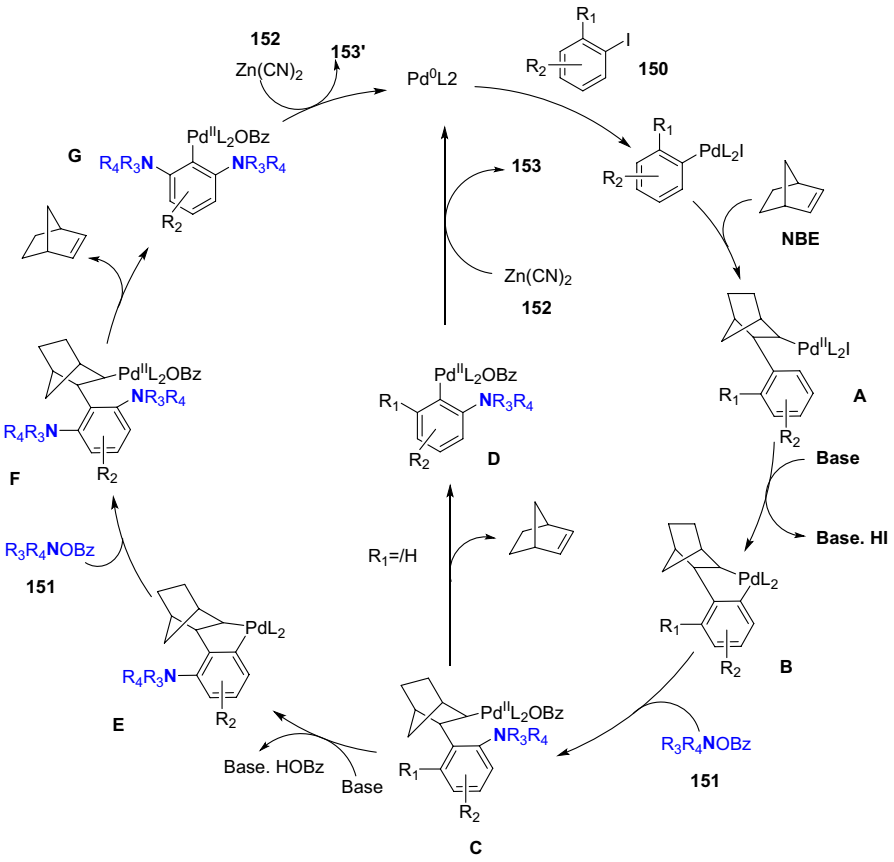
Scheme 59 Ranu's Pd/norbornene-catalyzed tandem C–H *ortho* amination/*ipso* cyanation strategy



Scheme 60 Hexa-substituted product formation



Scheme 61 Lauten's approach to *ortho*-amino benzonitriles

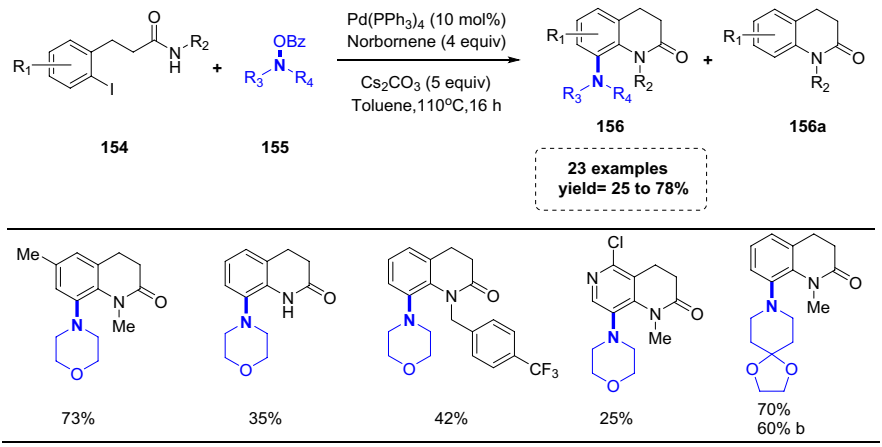


Scheme 62 Possible reaction mechanism for Lauten's strategy

five-membered Pd complex (**A**) via NBE insertion and C–H palladation which was formed by oxidative addition of 2-iodotoluene (**142**) with Pd (0). Subsequently, the generation of Pd (IV) complex (**B**) by the oxidative addition of Pd complex (**A**) with *O*-benzoyl hydroxylamine (**143**), further forms a C–N bond through reductive elimination. Finally, the Heck reaction of *ortho*-aminated Pd (II) species (**D**) formed by norbornene ejection of complex (**C**) and gave the final product (**145**).

In 2016, Ranu et al. [112] reported an *ortho* C–H amination followed by the terminal C–C cross-coupling/*ipso* cyanation of iodoarenes under Pd/norbornene catalysis to afford the respective 2-amino benzonitriles (**149**) (Scheme 59). Notably, this synthetic protocol provided Hexa-substituted product bearing two cyano and four amino functionalities under standard conditions (Scheme 60). The major advantage of this reaction was the wide substrate scope, mild reaction conditions, good functional group tolerance, and applicability on a gram scale with good yields.

Lauten's group [113] described Pd-catalyzed, norbornene-mediated synthesis of diverse *ortho*-aminated benzonitriles utilizing $Zn(CN)_2$ (**152**) as a terminating agent

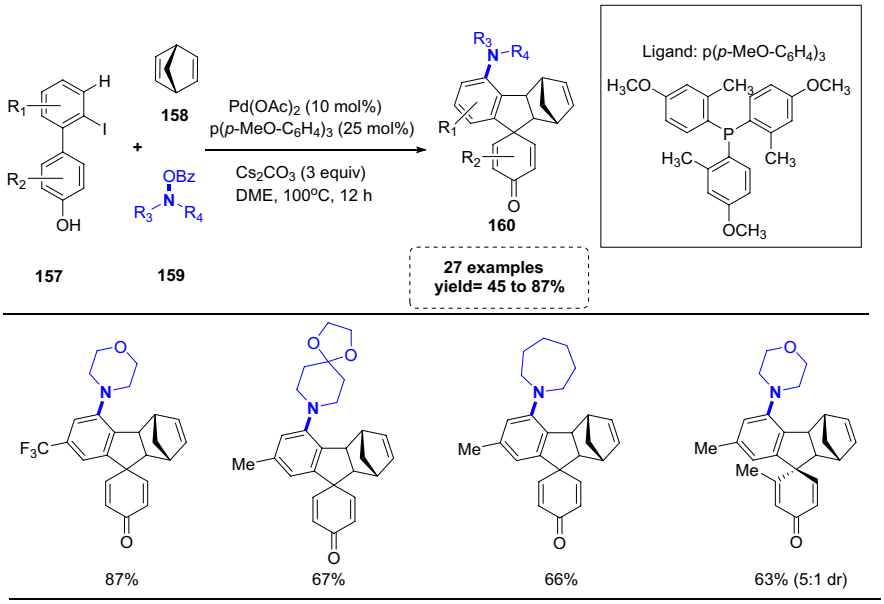


Scheme 63 Pd/norbornene-mediated Catellani reaction for the synthesis of diverse *ortho*-aminated dihydroquinolinones

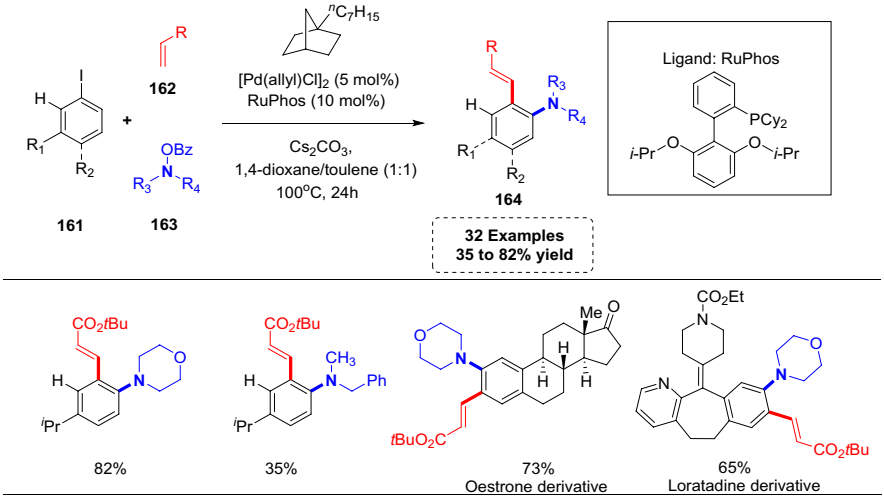
via tandem C–C and C–CN bond formation in the same year (Scheme 61). The same group reported the first example of the terminating agent with $Zn(CN)_2$ in 2006. The optimization studies indicated that the stoichiometric amount of norbornene and the selection of an appropriate bidentate ligand had a substantial impact on the reaction. A wide range of functional groups was compatible with this synthetic strategy and corresponding *O*-aminated benzonitrile (**153**) were obtained in good-to-excellent yields (29–93%).

The proposed catalytic cyclic is presented in Scheme 62. A five-membered Pd complex (**B**) was generated by oxidative addition and copalladation of norbornene which led to the formation of intermediate (**A**), followed by the base-assisted *ortho* C–H activation and HI elimination. Subsequently, the amination complex (**C**) was formed by direct *ortho* amination of Pd complex (**B**) via N–O bond cleavage. In the end, the elimination of norbornene followed by the *ipso* cyanation offered the final product along with the Pd (0). In the case of aryl iodides with no ortho substitution, repeated C–H activation at both *Ortho* positions of complex (**C**) may occur, resulting in the formation of a five-membered Pd complex (**E**) and an amination complex (**F**). Lastly, the final deaminated product was obtained by following the same pathway.

In the following year, the same group [114] described a novel method for the synthesis of diverse *ortho*-aminated dihydroquinolinones (**156**) via sequential intermolecular amination followed by intramolecular cyclization (Scheme 63). Several control experiments were performed to reduce the amount of by-product (**156a**) (intramolecular cyclization lacking *ortho*-amination) formation, suggesting that equiv. of norbornene and its ratio with a Pd catalyst plays a crucial role. The 4 equiv. of norbornene and 1:5 Pd:norbornene ratio were found to be optimal. Additionally, the formation of the by-product (**156a**) was preferential in more polar solvents. This reaction exhibits broad substrate scope and good functional group tolerance.

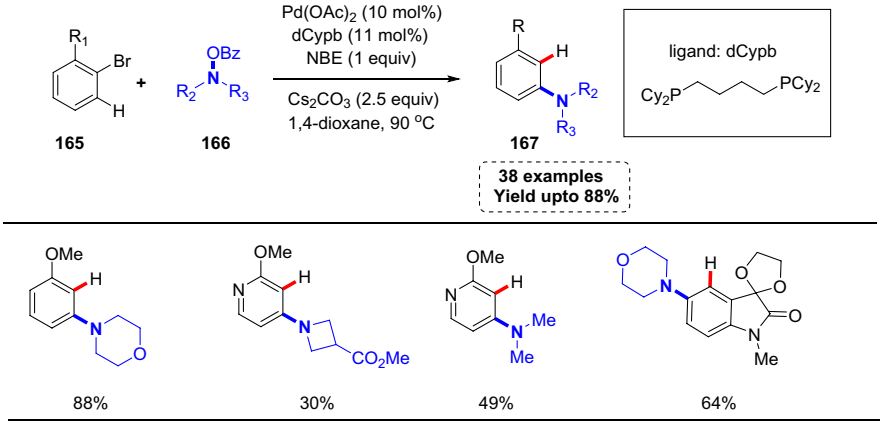


Scheme 64 Laun's Pd/NBD-catalyzed method to afford highly functionalized spiroindenes



Scheme 65 Dong's Pd/NBE-catalyzed coupling reaction to afford *ortho*/*ipso* functionalized arenes

In 2017, Luan et al. [115] reported a three-component coupling reaction to afford highly functionalized spiroindenes (**160**) via C–H amination and phenol dearomatization under the Pd/norbornadiene catalytic system (Scheme 64). This approach allowed the simultaneous formation of one C–N and two C–C bonds in a single transformation. A variety of bipohosphine ligands were evaluated with a Pd(OAc)2



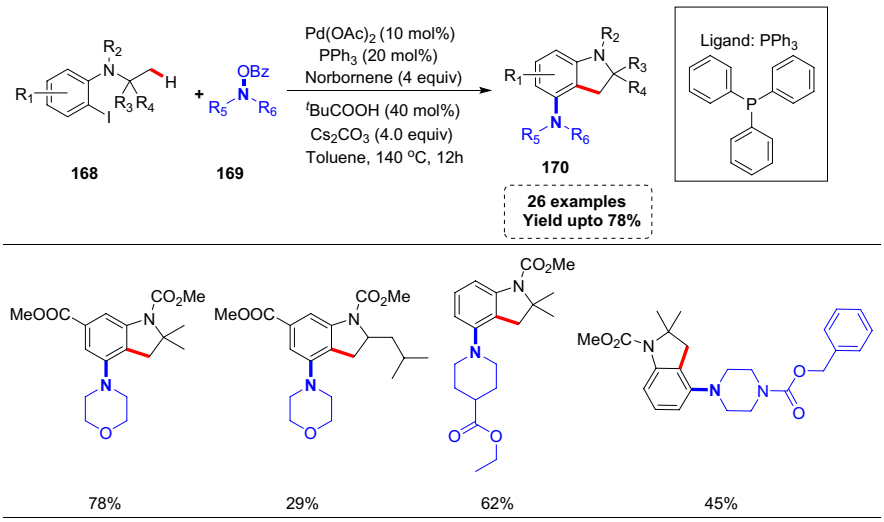
Scheme 66 Dong's Pd/NBE-catalyzed cross-coupling reaction strategy

catalyst to limit by-product creation; the electron-rich P(p-MeO-C6H4)$_3$ ligand was determined to be the best. Notably, asymmetric phenol could be accommodated in this reaction, yielding diastereo- and enantioselective spiroindenes.

In 2018, Dong's group [116] reported chemoselective mono *ortho* substitution of unsubstituted aryl iodides (**161**) (Catellani-type reaction) and ipso functionalization utilizing a newly designed norbornene co-catalyst that worked as cooperative with a Pd catalyst, which could avoid the *ortho* constraint (Scheme 65). Introducing a specific sterically hindered group at a bridgehead carbon of NBE (C_1 or C_4) could promote *β*-carbon elimination by destabilizing second C–H metalation in TS through the steric interaction between the R group of aryl iodide and *O*-benzoyl hydroxylamine (**163**) or with a ligand that would provide the mono *ortho*-substituted product. The alkyl group on bridgehead carbon of norbornene afforded the final products in good yields, and *n*-heptyl-substituted norbornene was found ideal. Several optimization studies suggested that Pd, norbornene, and ligand are essential for this transformation and the mixed solvent system proved superior to a single solvent. The synthetic utility of this protocol was explored by the selective *ortho*- amination of the drug oestrone and loratadine in good yields.

Dong et al. [117] described a multicomponent reaction in which they enhanced the reactivity of aryl bromides (**165**) by substituting different electrophiles (**167**) at the *ortho* position using Pd/norbornene catalysts (Scheme 66). Based on the mechanistic studies, it was found that this cross-coupling methodology worked for the *ipso*/*ortho* functionalization of aryl bromide. For *ortho* functionalization, this method performed well with amination, acylation, and alkylation. Also, they have reported alkynylation, arylation, and borylation of aryl bromides.

The Pd-catalyzed, norbornene-mediated *ortho* amination and C(sp3)-H arylation of unactivated alkanes (**168**) was achieved by Liang et al. [118] in 2018. After a series of optimization studies, they found that using a catalytic amount of pivalic acid as an additive could promote C–H activation of unactivated alkanes such as the C–H bond of the *tert*-butyl methyl group. Additionally, it could activate C–H bonds

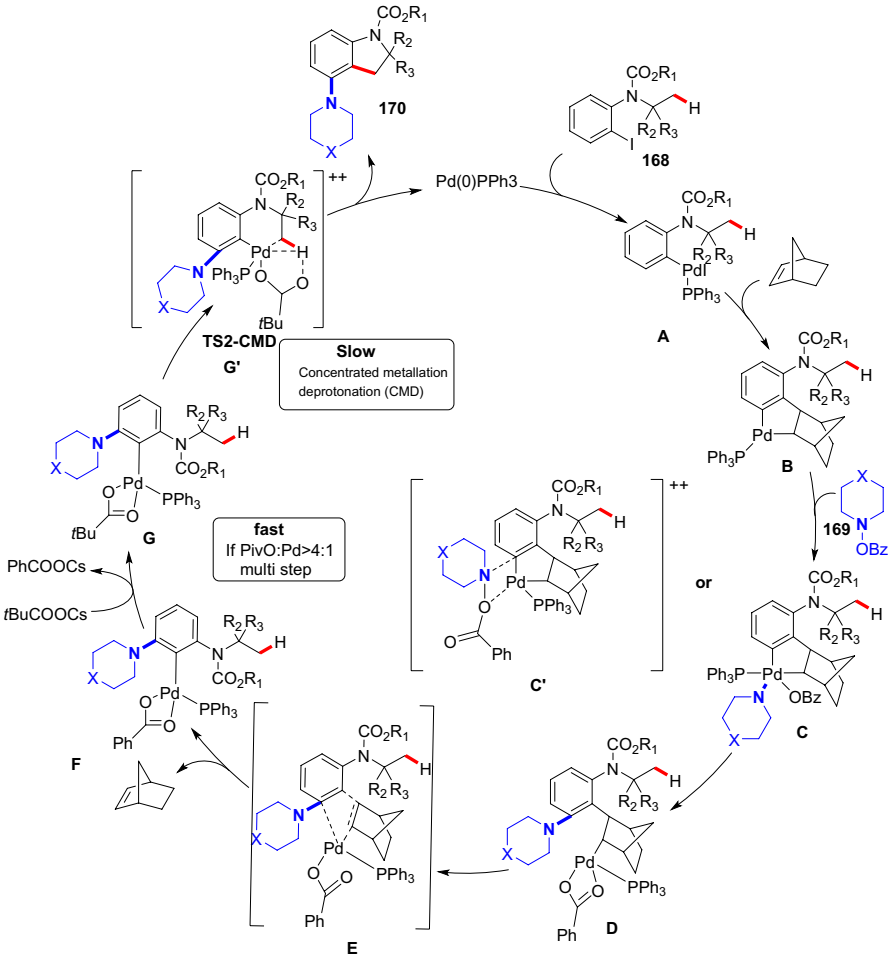


Scheme 67 Pd norbornene-catalyzed *ortho* amination and C(sp3)-H arylation of unactivated alkanes

of other groups such as isopropyl, isoamyl, isobutyl, etc. *O*-iodianiles with various alkane groups as well as neutral and electron-withdrawing groups on aromatic rings underwent the reaction smoothly, However, electron-donating groups could not yield the desired product (Scheme 67).

The mechanistic hypothesis for this *ortho* amination and C(sp3)-H arylation is described below (Scheme 68). The traditional oxidative addition of Pd(0) to iodobenzene (**168**) (intermediate **A**) and norbornene insertion followed by oxidative C–H activation generates ANP intermediate (**B**). Following the oxidative addition of *N*-benzoyloxyamine (**169**) to the intermediate (**B**), Pd (IV) intermediate (**C**) was formed. Next, ortho-aminated arene intermediate (**D**) was obtained by reductive elimination. Direct electrophilic amination of *N*-benzoyloxyamine (**169**) with ANP intermediate (**B**) may also produce ortho-aminated arene intermediate (**D**). Further, the *β*-C elimination of intermediate (**D**) yielded the k^2-benzoic acid intermediate (**F**). When the pivalic acid/Pd ratio surpasses 4:1[23], a quick acid exchange can build a 2-pivalic acid intermediate (**G**) by substituting benzoic acid with cesium pivalate created in situ from pivalic acid and Cs_2CO_3. Finally, intermediate (**G**) is deprotonated via a CMD process, yielding intermediate (**G′**), which is then reductively eliminated to get the desired product (**170**).

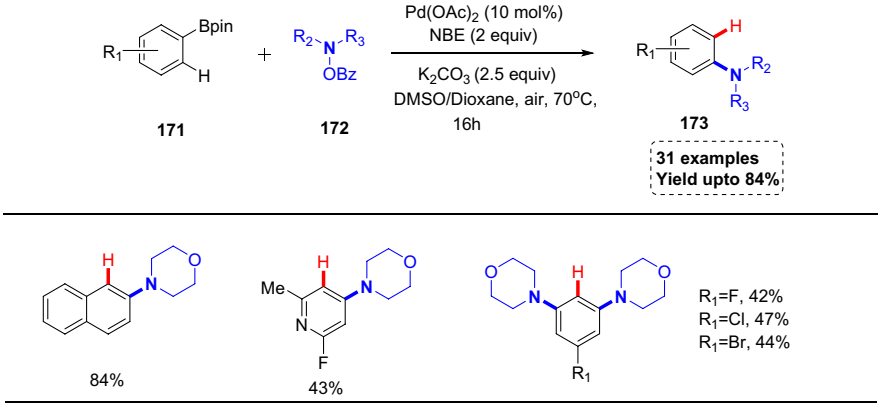
Chen et al. [119] reported palladium/norbornene co-operative catalysis selective redox neutral *ipso* protonation followed by *ortho* C–H amination of pinacol aryl borates (**171**) with the help of amine benzoates (**172**) (Scheme 69). The redox-neutral *ipso* protonation of this transformation was confirmed by preliminary deuterium-labeled experiments. The synthetic utility of this reaction was explored by performing a scale-up experiment (9 mmol) and by synthesizing EphB4 kinase inhibitors in good yields. It is worth noting that the presence of air may help the reaction by preventing other Pd-catalyzed side reactions and enhancing the yield.



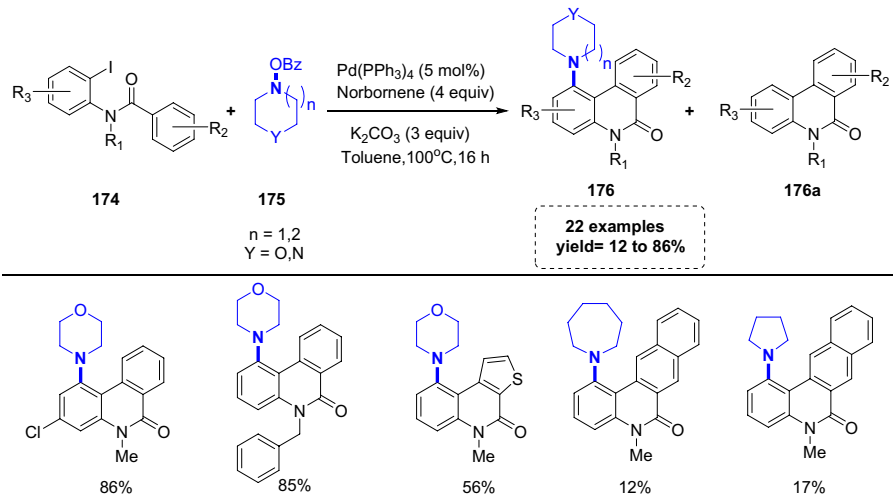
Scheme 68 The mechanistic hypothesis for this *ortho* amination and C(sp3)-H arylation

In 2020, Lauten et al. [120] described the Catellani reaction for the synthesis of aminated phenanthridinones (**176**) via *ortho*-amination followed by *ipso*-C–H arylation. This single-step procedure provides a novel strategy for the synthesis of substituted aminated phenanthridinones as shown in Scheme 70 [59]. The optimization studies indicated that base K_2CO_3 plays an important role in *ortho*-amination and intramolecular cyclization. Hydroxylamines other than piperazine and morpholine delivered the products in relatively low yields.

A postulated reaction course is shown in Scheme 71. Initially, the palladcycle-I (step A) would be generated by successive oxidative addition of benzamide (**174**) to Pd (0), followed by, the insertion of norbornene resulting in intermediate-II (Step B). Further, a base K_2CO_3-assisted concentration metalation process (CMD) gives aryl-norbornyl-palladacylcle (ANP) III (Step C) as a key

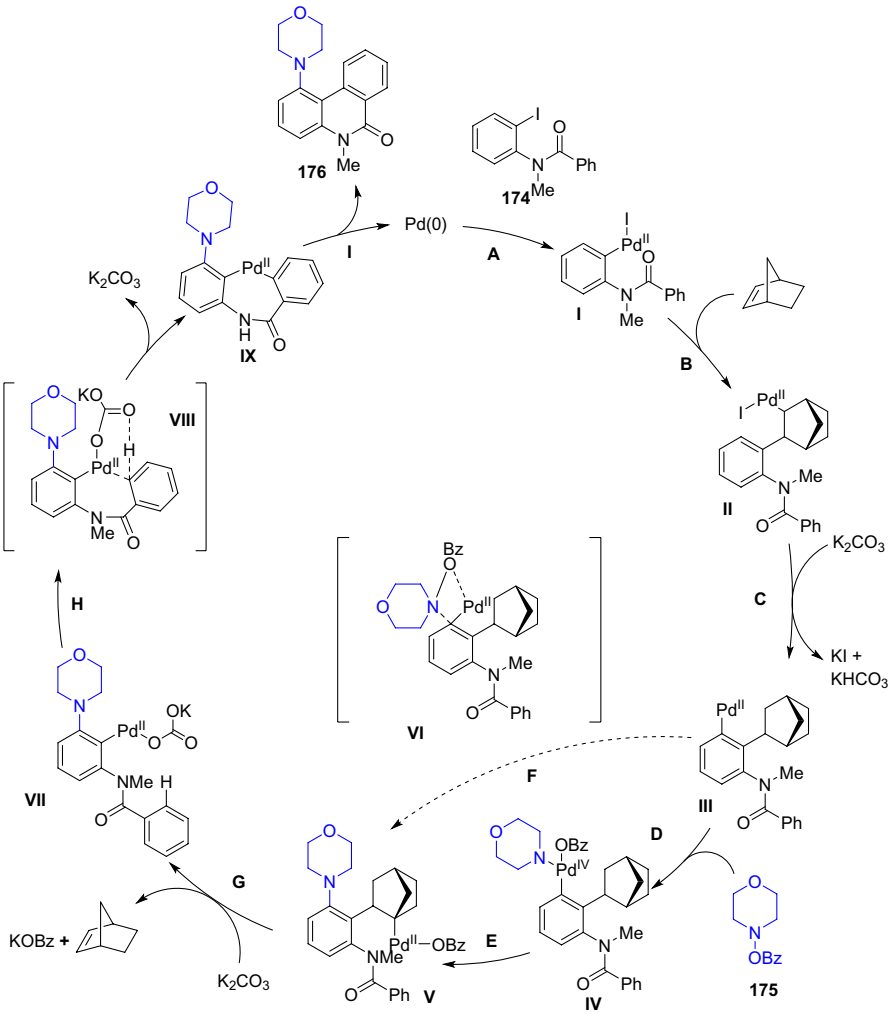


Scheme 69 Chen's redox neutral C–H amination of pinacol aryl borates



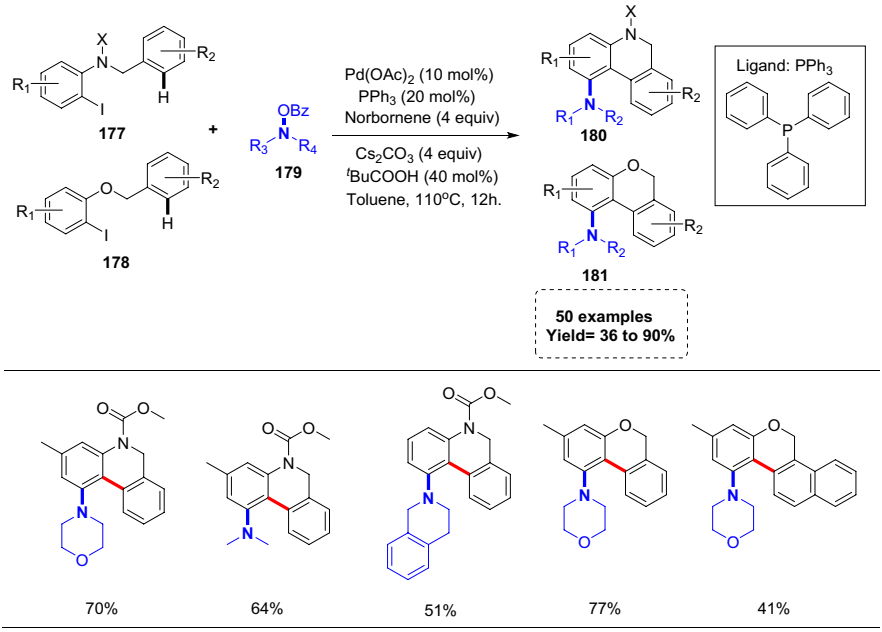
Scheme 70 Lauten's Pd/norbornene-catalyzed protocol for the synthesis of aminated phenanthridinones

intermediate. Subsequently, oxidative addition of intermediate III (Step C) with hydroxylamine (**175**) transformed the Pd(II) species into Pd(IV) intermediate IV (Step D), which underwent reductive elimination to produce amination complex V (Step E). On the other hand, the direct electrophilic amination mechanism could also be responsible for amination complex VI (Step F). Next, the Pd (II) species VII (Step G) resulting from expulsion of norbornene underwent second base K_2CO_3-assisted concentration metalation process (CMD) as shown in transition state VIII (Step H), generating the seven-membered palladacycle IX, followed by reductive elimination afforded the final product (**176**) (Step I) with the regeneration of the catalyst.

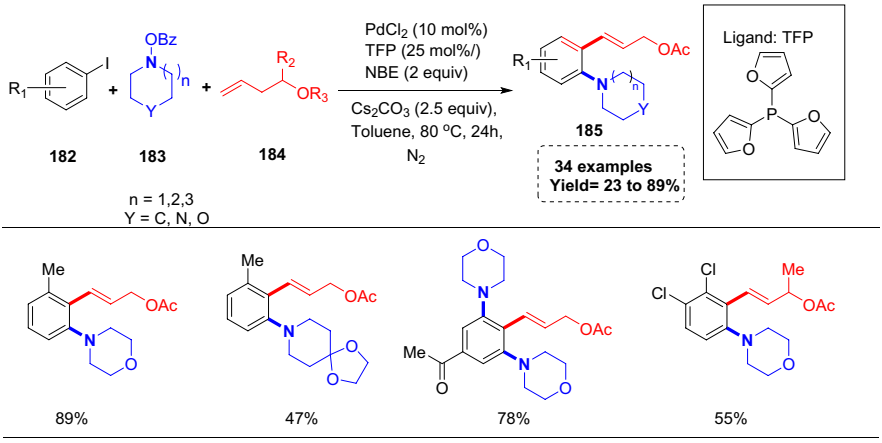


Scheme 71 Proposed reaction course for Lauten's methodology

In 2020, another Pd-catalyzed, norbornene-mediated synthesis of various dihydrophenanthridines (**180**), phenanthridines, and 6*H*-benzo[*c*] chromenes (**181**) was reported by Liang and coworkers [121] (Scheme 72). The reaction proceeds with benzyl carbamate (**177**) and *O*-benzoyl hydroxylamines (**179**) through Catellani *ortho*-amination and unactivated C–H arylation. Most of the benzyl carbamates with various substitutions performed well, leading to broad substrate scope. Due to steric hindrance, substitution at *para* position concerning *o*-iodoanilines failed to deliver the final product. Additionally, both cyclic and acyclic hydroxylamines underwent the reaction and afforded the corresponding products with moderate-to-good yields. The possible reaction mechanism may involve norbornene insertion, formation of



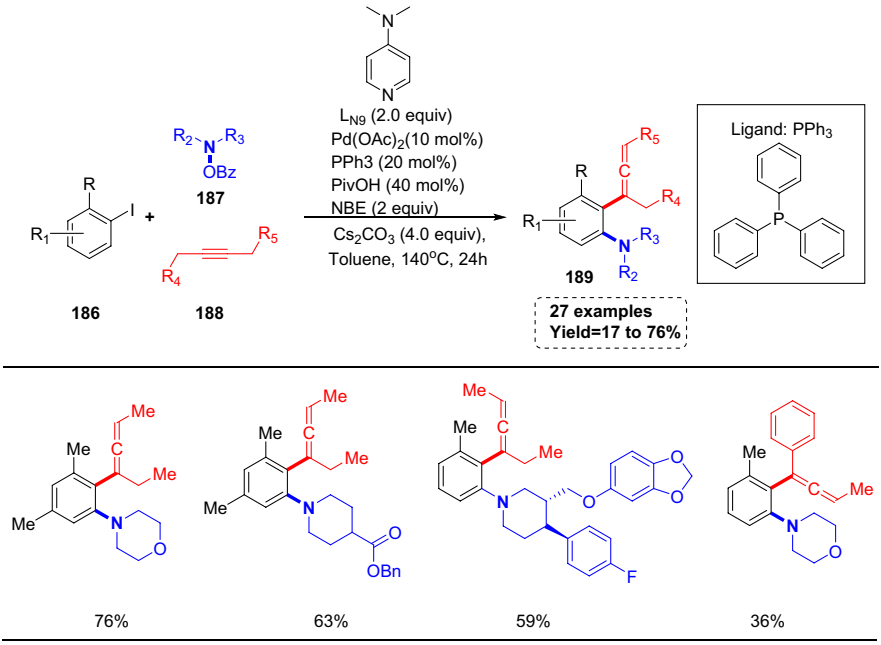
Scheme 72 Pd/NBE-mediated synthesis of various dihydrophenanthridines, phenanthridines, and 6*H*-benzo[*c*] chromenes



Scheme 73 Cheng's Pd/norbornene Catellani-type reaction method to construct 2-aminocinnamyl ester derivatives

palladacycle, oxidative addition, and reductive elimination as described earlier in this article.

In 2020, Cheng et al. [122] disclosed a Pd-catalyzed three-component Catellani-type reaction of haloarenes (**182**), *O*-benzoylhydroxylamine (**183**), and allylic esters

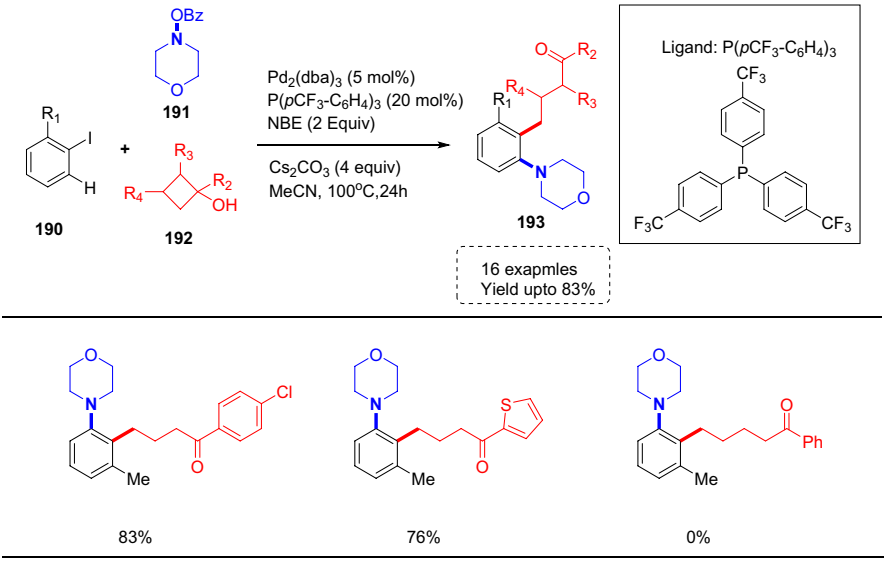


Scheme 74 Liang's Pd/NBE-mediated *ortho* C–H amination and *ipso* functionalization strategy

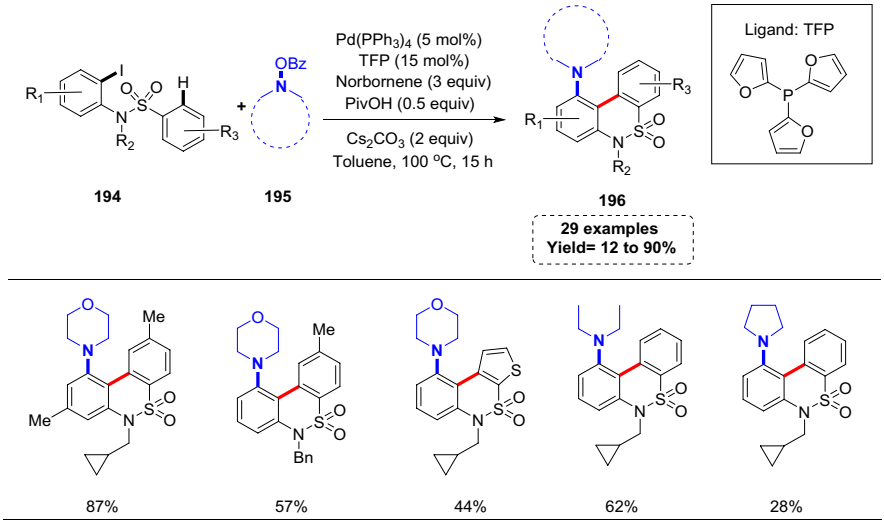
(**184**). This one-pot amination strategy provided multiple functionalized 2-aminocinnamyl ester derivatives (**185**) via sequential electrophilic C–H amination and Heck-type termination using allyl esters as a terminating agent. Chemo selectivity and good functional group compatibility provided good applicability to this reaction. However, acyclic amination reagents were not feasible under standard conditions, and the diaminated products were obtained when *para*-substituted aryl halides were employed (Scheme 73).

In the same year, Liang et al. [123] reported the novel *ortho* C–H amination and *ipso* functionalization strategy of aryl iodides (**186**) aided by DMAP and PivOH using Pd/norbornene catalytic system, *O*-hydroxylamines (**187**) as an aminating reagent, and terminal alkynes (**188**) as an allenization agent (Scheme 74). After a series of control experiments, it was concluded that the triphenylphosphine or bidentate ligand, as well as the base, were crucial for this transformation. Notably, the reaction has been affected by the nature of the alkyl substituent, which selectively drives on alkane in the presence of an aromatic group present on the other side of the alkyl substituent. The mechanistic pathway suggested that the allenization could be promoted by concentrated metalation deprotonation (CMD) and β-hydrogen elimination.

Carbon–carbon σ-bonds cleavage has been a prodigious task in organic chemistry, since its thermal stability and kinetic inertness. In this regard, Liang and coworkers [124] investigated a new and simple approach for exploiting the cyclobutanol (**192**) as a terminating agent via the ring-opening process in the Catellani reaction. The reaction involves β-carbon elimination followed by electrophilic amination with

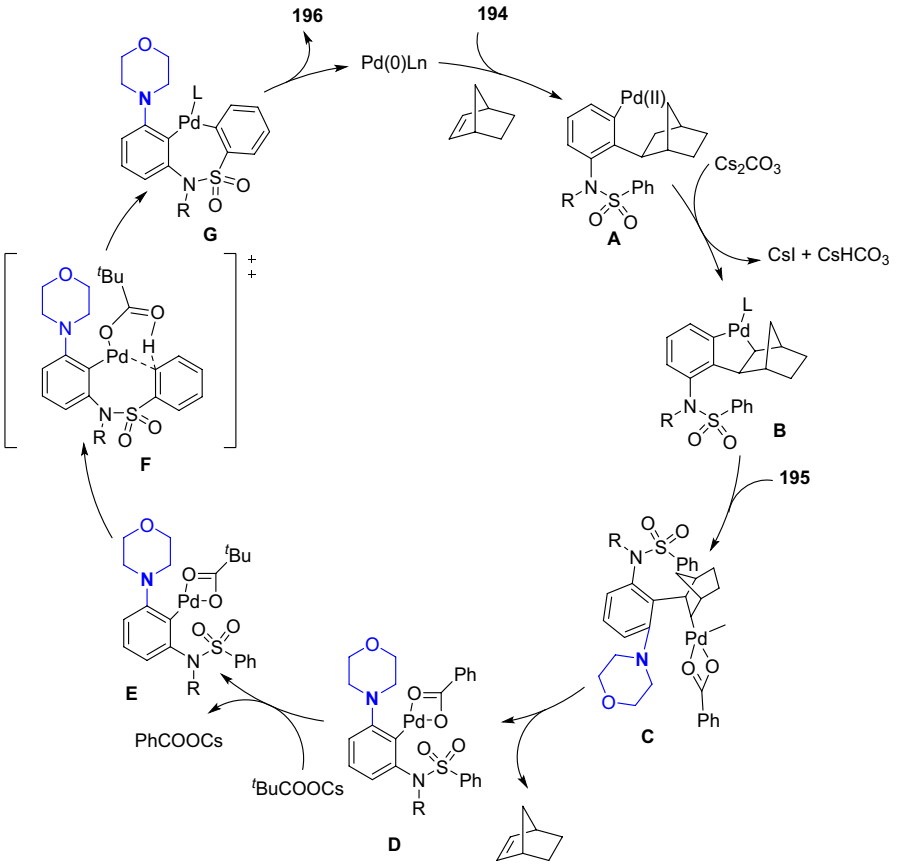


Scheme 75 Pd-catalyzed amination cross-coupling reaction from aryl halide, *O*-benzoylhydroxylamine, and cyclobutanol



Scheme 76 Sun's Pd/NBE-catalyzed *ortho* C–H amination and *ipso* arylation strategy to afford diverse benzosultams

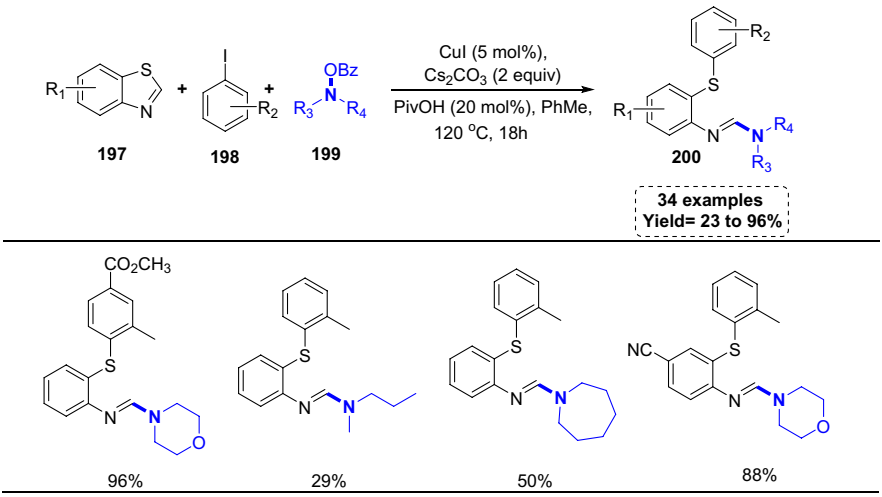
O-benzoyl hydroxylamine (**191**) under Pd/NBE cooperative catalysis (Scheme 75). Notably, the phenyl-substituted cyclobutanol did not undergo the reaction. This reaction opened a new platform for the preparation of novel polysubstituted hydrocarbons (**190**) in good-to-excellent yields.



Scheme 77 The possible catalytic cycle for *ortho* C–H amination and *ipso* arylation

In 2021, Sun et al. [125] reported the Pd-catalyzed, norbornene-mediated protocol to afford structurally diverse benzosultams (**196**) via sequential *ortho* C–H amination and *ipso* arylation of sulfonamide tethered aryl iodides (**194**) (Scheme 76). To understand the role of ligands several ligands were examined, and it was found that the tri-2-furylphosphine (TFP) gave optimal yields, which was further enhanced by the addition of pivalic acid as an additive. The reaction exhibited excellent functional group compatibility, however, sterically hindered and pyrrolidine-based hydroxylamines might result in lower yields.

The possible catalytic cycle is depicted in Scheme 77. The successive oxidative addition of (**194**) to Pd(0) gives Pd(II) species (**A**). Insertion of norbornene, and base-mediated *ortho* C–H activation produce crucial aryl-norbornyl-palladacycle (**B**). Subsequently, two possible reaction pathways could reach intermediate Pd(IV) species (**D**) in the presence of N-based oxidant (*O*-benzoyl hydroxylamines) (**195**). Path A provided cyclic Pd (IV) complex (intermediate **B**) by oxidative addition and then reductive elimination afforded Pd (II) species (Intermediate **C**). It could also be



Scheme 78 Cu(I)-catalyzed redox-neutral electrophilic ring-opening amination of benzothiazoles

achieved by path B through direct electrophilic substitution. After the liberation of norbornene, K^2 benzoic acid (intermediate **D**) was formed via *β*-carbon elimination. The reaction between PivOH and base Cs_2CO_3 gives cesium pivalate which replaces benzoic acid rapidly to deliver (intermediate **E**). This intermediate E, further undergoes acid-initiated CMD leading to the formation of (intermediate **G**) through transition state (**F**). Finally, reductive elimination provides desired product (**196**) and regeneration of Pd(0).

2.8 Ring-Opening Reactions

In 2020, Liang's group [126] demonstrated electrophilic ring-opening amination of benzothiazoles. This redox-neutral, one-spot ring-opening process yielded a variety of 1-amino-N-(2-(phenylthio)phenyl)methanimines (**200**) (Scheme 78). In this reaction, C–S and N–O bonds are cleaved, and new C–S and C–N bonds are formed in one spot fashion. Furthermore, benzoxazole could undergo this ring-opening reaction with modified conditions. The mechanistic study showed that the chemical route may include the Heck reaction and a secondary amine intermediate combination, but it eliminates the free radical method and benzothiazole dehydroisomerization mechanism.

3 Conclusions

In conclusion, electrophilic amination using *O*-benzoylhydroxylamines has become a straightforward and practical way for the construction of C–N bonds. In this review, we have highlighted some of the important recent advances in

O-benzoylhydroxylamine involving electrophilic amination methods for the construction of C–N bond, which could be exploited to build various pharmaceutically important nitrogen-containing heterocycles. Furthermore, we categorically mentioned the significance, challenges, and future scope of *O*-benzoylhydroxylamine.

3.1 Significance and Applications

i. One of the long-standing study areas in synthetic organic chemistry has been the addition of nitrogen functionality to carbon skeletons and the development of C–N bond-forming processes. Particularly, the transition metal-catalyzed addition-type reaction is attractive because it converts simple alkenes and alkynes into medicinally important N-containing molecules.
ii. Utilizing the nitrogen umpolung concept, the fundamental nitrogen of the amino group can serve as the nitrogen electrophile to accomplish challenging amino functionalization like hydroamination, aminoboration, and carboamination in conjunction with the hydride, boryl, and carbon external nucleophiles, respectively.
iii. An efficient enantioselective induction in various organic moieties is accomplished by the appropriate choice of catalysts and ligand combinations. This would produce intricate alkylamines or arylamines of important pharmacological and therapeutic utility.
iv. Cu, Pd, and Ni are used as the most common transition metals for electrophilic amination through ortho-C–H activation, C–H amination, and Catellani-type reactions to offer various amino functionalized compounds and diverse difunctionalized anilines.
v. The normally challenging synthesis of sterically hindered α-branched aniline is made much easier by the iron-based catalytic method. Asymmetric catalysis is still being developed though.
vi. Other transition metals, such as Rh, and Ru, have also been reported for these transformations. However, they have received less attention.

3.2 Challenges

Despite the significant advances in this field, there are still several challenges or gaps that need to be addressed in the future.

i. One of the major obstacles encountered in electrophilic amination, especially Cu-catalyzed hydroamination, is electrophile reduction side reaction leading to reduced yields or resulting in no product formation.
ii. The scope for hydroxylamine electrophile is still limited to *N*,*N*-dialkyl amines, or *O*-acylated hydroxylamine. Furthermore, the direct use of primary amino groups (R2N-X) as an electrophilic amination reagent still needs to

be addressed because of the widespread occurrence of chiral primary amino groups in medicine and bioactive compounds.

iii. Enhancement in the regioselectivity of sterically and electronically unbiased or less biased internal alkenes.

iv. Only copper catalysts have been utilized in aminoboration reactions, and the range of intramolecular aminoboration is still restricted to simple alkenes. To broaden the focus and address the remaining issues, the development of different and versatile amino-boration catalysts with other transition metals may pave way for the discovery of new synthetic methodologies.

v. 8-amino quinoline as a directing group is extensively used for Ni-catalyzed hydroamination reactions. However, further research is still required on the usage of other directing groups. Nowadays, for many alkene substrates, free alcohol, amine, and ketones can serve as a directing group. In light of this, it is preferable to use those functional groups as directing groups.

vi. It is still difficult to achieve a fully intermolecular three-component coupling in palladium-catalyzed aza-Heck reaction-enabled carboamination. Additionally, in Co-based catalyst systems, the scope of electrophilic amination reagents is limited to only diazo compounds. Additional development of amine partners is strongly anticipated.

3.3 Future Scope

The aforementioned challenge would be accomplished by additional rational design of catalyst, electrophilic amination agents, and external nucleophiles. Additionally, using proper directing groups and chiral ligands might increase the regioselectivity of sterically hindered unactivated, or less activated alkenes.

We predict that in the future, umpolung strategy-based aminative difunctionalization reactions will be developed, opening the door to the discovery of novel N-containing drugs and valuable chemical compounds. One of the most effective and practical synthetic tools in the amination toolkit is expected to be *O*-benzoylhydroxylamines, and in the near future we might expect to see many additional developments of unique approaches. This elaborate and extensive review will benefit several researchers in this field to find and address the gaps by developing more efficient synthetic strategies.

Acknowledgements The authors are thankful to the Discipline of Pharmaceutical Sciences, College of Health Sciences, University of Kwa-Zulu Natal (UKZN), Durban, South Africa, for providing all the necessary facilities. R.K. gratefully acknowledges National Research Foundation-South Africa for funding this project (Grant No. 129247).

Data availability This work is review article, and as such, readers will need to contact referenced authors to obtain additional information regarding the data presented.

Declarations

Conflict of interest The reported work is acknowledged/cited, with no potential conflicts of interest.

References

1. Zhao Y, Xia W (2018) Recent advances in radical-based C–N bond formation: via photo-/electrochemistry. Chem Soc Rev 20:20
2. Wang Q, Su Y, Li L, Huang H (2016) Transition-metal catalysed C–N bond activation. Chem Soc Rev 20:20
3. Zheng YN, Zheng H, Li T, Wei WT (2021) Recent advances in copper-catalyzed C−N bond formation involving N-centered radicals. Chemsuschem 20:20
4. Collet F, Lescot C, Dauban P (2011) Catalytic C–H amination: the stereoselectivity issue. Chem Soc Rev. https://doi.org/10.1039/c0cs00095g
5. Jeffrey JL, Sarpong R (2013) Intramolecular C(sp3)–H amination. Chem Sci. https://doi.org/10.1039/c3sc51420j
6. Lu Z, Ma S (2008) Metal-catalyzed enantioselective allylation in asymmetric synthesis. Angew Chem Int Ed 20:25
7. Barker TJ, Jarvo ER (2011) Developments in transition-metal-catalyzed reactions using electrophilic nitrogen sources. Synthesis (Stuttg) 20:25
8. Wang C (2020) Development of transition-metal-catalysed cross-coupling reactions through ammonium C–N bond cleavage. Chem Pharm Bull 25:25
9. Goodbrand HB, Hu NX (1999) Ligand-accelerated catalysis of the Ullmann condensation: application to hole-conducting triarylamines. J Org Chem. https://doi.org/10.1021/jo981804o
10. Strieter ER, Blackmond DG, Buchwald SL (2005) The role of chelating diamine ligands in the Goldberg reaction: a kinetic study on the copper-catalyzed amidation of aryl iodides. J Am Chem Soc. https://doi.org/10.1021/ja050120c
11. Klapars A, Huang X, Buchwald SL (2002) A general and efficient copper catalyst for the amidation of aryl halides. J Am Chem Soc. https://doi.org/10.1021/ja0260465
12. Bruno NC, Tudge MT, Buchwald SL (2013) Design and preparation of new palladium precatalysts for C-C and C–N cross-coupling reactions. Chem Sci. https://doi.org/10.1039/c2sc20903a
13. Roizen JL, Harvey ME, Du BJ (2012) Metal-catalyzed nitrogen-atom transfer methods for the oxidation of aliphatic C–H bonds. Acc Chem Res. https://doi.org/10.1021/ar200318q
14. Simon RC, Grischek B, Zepeck F et al (2012) Regio- and stereoselective monoamination of diketones without protecting groups. Angew Chem Int Ed. https://doi.org/10.1002/anie.201202375
15. Simon RC, Grischek B, Zepeck F et al (2012) Regio- and stereoselective monoamination of diketones without protecting groups. Angew Chem. https://doi.org/10.1002/ange.201202375
16. Campbell AN, Stahl SS (2012) Overcoming the 'oxidant problem': strategies to use O2 as the oxidant in organometallic C–H oxidation reactions catalyzed by Pd (and Cu). Acc Chem Res. https://doi.org/10.1021/ar2002045
17. Gephart RT, Warren TH (2012) Copper-catalyzed sp3 C-H amination. Organometallics 25:24
18. Louillat ML, Patureau FW (2014) Oxidative C-H amination reactions. Chem Soc Rev 25:45
19. Yan X, Yang X, Xi C (2014) Recent progress in copper-catalyzed electrophilic amination. Catal Sci Technol 20:25
20. Erdik E, Ay M (1989) Electrophilic amination of carbanions. Chem Rev. https://doi.org/10.1021/cr00098a014
21. Daşkapan T (2011) Synthesis of amines by the electrophilic amination of organomagnesium,-zinc,-copper, and-lithium reagents. ARKIVOC. https://doi.org/10.3998/ark.5550190.0012.520
22. Dong X, Liu Q, Dong Y, Liu H (2017) Transition-metal-catalyzed electrophilic amination: application of *O*-benzoylhydroxylamines in the construction of the C−N bond. Chem A Eur J 20:25
23. Berman AM, Johnson JS (2004) Copper-catalyzed electrophilic amination of diorganozinc reagents. J Am Chem Soc. https://doi.org/10.1021/ja049474e

24. Cho SH, Kim JY, Kwak J, Chang S (2011) Recent advances in the transition metal-catalyzed two-fold oxidative C–H bond activation strategy for C–C and C–N bond formation. Chem Soc Rev. https://doi.org/10.1039/c1cs15082k
25. Bariwal J, Van Der Eycken E (2013) C-N bond forming cross-coupling reactions: an overview. Chem Soc Rev 20:525
26. Beccalli EM, Broggini G, Martinelli M, Sottocornola S (2007) C-C, C-O, C-N bond formation on sp2 carbon by Pd(II)-catalyzed reactions involving oxidant agents. Chem Rev 25:25
27. Luo J, Wei WT (2018) Recent Advances in the construction of C–N bonds through coupling reactions between carbon radicals and nitrogen radicals. Adv Synth Catal 25:45
28. Campbell MJ, Johnson JS (2007) Mechanistic studies of the copper-catalyzed electrophilic amination of diorganozinc reagents and development of a zinc-free protocol. Org Lett. https://doi.org/10.1021/ol0702829
29. McDonald SL, Wang Q (2014) Copper-catalyzed α-amination of phosphonates and phosphine oxides: a direct approach to α-amino phosphonic acids and derivatives. Angew Chem. https://doi.org/10.1002/ange.201308890
30. Rucker RP, Whittaker AM, Dang H, Lalic G (2012) Synthesis of hindered anilines: copper-catalyzed electrophilic amination of aryl boronic esters. Angew Chem Int Ed. https://doi.org/10.1002/anie.201200480
31. Müller TE, Hultzsch KC, Yus M et al (2008) Hydroamination: direct addition of amines to alkenes and alkynes. Chem Rev. https://doi.org/10.1021/cr0306788
32. Gooßen LJ, Huang L, Arndt M et al (2015) Late transition metal-catalyzed hydroamination and hydroamidation. Chem Rev 25:25
33. Johns AM, Sakai N, Ridder A, Hartwig JF (2006) Direct measurement of the thermodynamics of vinylarene hydroamination. J Am Chem Soc. https://doi.org/10.1021/ja062773e
34. Müller TE, Beller M (1998) Metal-initiated amination of alkenes and alkynes. Chem Rev. https://doi.org/10.1021/cr960433d
35. Seebach D, Corey EJ (1975) Generation and synthetic applications of 2-lithio-1,3-dithianes. J Org Chem. https://doi.org/10.1021/jo00890a018
36. Seebach D (1979) Methods of reactivity umpolung. Angew Chem Int Ed English 25:25
37. Miki Y, Hirano K, Satoh T, Miura M (2013) Copper-catalyzed intermolecular regioselective hydroamination of styrenes with polymethylhydrosiloxane and hydroxylamines. Angew Chem Int Ed. https://doi.org/10.1002/anie.201304365
38. Zhu S, Niljianskul N, Buchwald SL (2013) Enantio- and regioselective CuH-catalyzed hydroamination of alkenes. J Am Chem Soc. https://doi.org/10.1021/ja4092819
39. Miki Y, Hirano K, Satoh T, Miura M (2014) Copper-catalyzed enantioselective formal hydroamination of oxa- and azabicyclic alkenes with hydrosilanes and hydroxylamines. Org Lett. https://doi.org/10.1021/ol5003219
40. Niljianskul N, Zhu S, Buchwald SL (2015) Enantioselective synthesis of α-aminosilanes by copper-catalyzed hydroamination of vinylsilanes. Angew Chem. https://doi.org/10.1002/ange.201410326
41. Shi SL, Buchwald SL (2015) Copper-catalysed selective hydroamination reactions of alkynes. Nat Chem. https://doi.org/10.1038/nchem.2131
42. Niu D, Buchwald SL (2015) Design of modified amine transfer reagents allows the synthesis of α-chiral secondary amines via CuH-catalyzed hydroamination. J Am Chem Soc. https://doi.org/10.1021/jacs.5b05446
43. Ichikawa S, Zhu S, Buchwald SL (2018) A modified system for the synthesis of enantioenriched N-arylamines through copper-catalyzed hydroamination. Angew Chem Int Ed. https://doi.org/10.1002/anie.201803026
44. Feng S, Hao H, Liu P, Buchwald SL (2020) Diastereo- and enantioselective CuH-catalyzed hydroamination of strained trisubstituted alkenes. ACS Catal. https://doi.org/10.1021/acscatal.9b04871
45. Ichikawa S, Buchwald SL (2019) Asymmetric synthesis of γ-amino alcohols by copper-catalyzed hydroamination. Org Lett. https://doi.org/10.1021/acs.orglett.9b03356
46. Takata T, Nishikawa D, Hirano K, Miura M (2018) Synthesis of α-aminophosphines by copper-catalyzed regioselective hydroamination of vinylphosphines. Chem A Eur J. https://doi.org/10.1002/chem.201802491
47. Yang Q, Li S, Wang J (2020) Asymmetric synthesis of chiral chromanes by copper-catalyzed hydroamination of 2H-chromenes. ChemCatChem. https://doi.org/10.1002/cctc.202000601

48. Takata T, Hirano K, Miura M (2019) Synthesis of α-trifluoromethylamines by Cu-catalyzed regio- and enantioselective hydroamination of 1-trifluoromethylalkenes. Org Lett. https://doi.org/10.1021/acs.orglett.9b01471
49. Nishino S, Miura M, Hirano K (2021) An umpolung-enabled copper-catalysed regioselective hydroamination approach to α-amino acids. Chem Sci. https://doi.org/10.1039/d1sc03692k
50. Jeon J, Lee C, Seo H, Hong S (2020) NiH-catalyzed proximal-selective hydroamination of unactivated alkenes. J Am Chem Soc. https://doi.org/10.1021/jacs.0c10333
51. Lee C, Seo H, Jeon J, Hong S (2021) γ-Selective C(sp3)–H amination via controlled migratory hydroamination. Nat Commun. https://doi.org/10.1038/s41467-021-25696-z
52. Lee C, Kang H-J, Seo H, Hong S (2022) Nickel-catalyzed regio- and enantioselective hydroamination of unactivated alkenes using carbonyl directing groups. J Am Chem Soc 144:9091–9100. https://doi.org/10.1021/jacs.2c02343
53. Yang D, Huang H, Zhang H et al (2021) Regioselective intermolecular hydroamination of unactivated alkenes: 'co-H' enabled remote functionalization. ACS Catal. https://doi.org/10.1021/acscatal.1c00625
54. Matsuda N, Hirano K, Satoh T, Miura M (2013) Regioselective and stereospecific copper-catalyzed aminoboration of styrenes with bis(pinacolato)diboron and *O*-benzoyl-*N*,*N*-dialkylhydroxylamines. J Am Chem Soc 20:25. https://doi.org/10.1021/ja4007645
55. Sakae R, Matsuda N, Hirano K et al (2014) Highly stereoselective synthesis of (borylmethyl)cyclopropylamines by copper-catalyzed aminoboration of methylenecyclopropanes. Org Lett. https://doi.org/10.1021/ol5001507
56. Sakae R, Hirano K, Satoh T, Miura M (2015) Copper-catalyzed stereoselective aminoboration of bicyclic alkenes. Angew Chem. https://doi.org/10.1002/ange.201409104
57. Sakae R, Hirano K, Miura M (2015) Ligand-controlled regiodivergent Cu-catalyzed aminoboration of unactivated terminal alkenes. J Am Chem Soc. https://doi.org/10.1021/jacs.5b02775
58. Kato K, Hirano K, Miura M (2017) Copper/bisphosphine catalysts in the internally borylative aminoboration of unactivated terminal alkenes with bis(pinacolato)diboron. J Org Chem. https://doi.org/10.1021/acs.joc.7b01874
59. Kato K, Hirano K, Miura M (2018) Copper-catalyzed regio- and enantioselective aminoboration of unactivated terminal alkenes. Chem A Eur J. https://doi.org/10.1002/chem.201801070
60. Gao DW, Gao Y, Shao H et al (2020) Cascade CuH-catalysed conversion of alkynes into enantioenriched 1,1-disubstituted products. Nat Catal. https://doi.org/10.1038/s41929-019-0384-6
61. Hemric BN, Chen AW, Wang Q (2019) Copper-catalyzed 1,2-amino oxygenation of 1,3-dienes: a chemo-, regio-, and site-selective three-component reaction with o-acylhydroxylamines and carboxylic acids. ACS Catal. https://doi.org/10.1021/acscatal.9b03076
62. Li Z, Zhang M, Zhang Y et al (2019) Multicomponent cyclopropane synthesis enabled by Cu-catalyzed cyclopropene carbometalation with organoboron reagent: enantioselective modular access to polysubstituted 2-arylcyclopropylamines. Org Lett. https://doi.org/10.1021/acs.orglett.9b01650
63. Zhang Y, Li Y, Zhou W et al (2020) Assembly of polysubstituted chiral cyclopropylamines via highly enantioselective Cu-catalyzed three-component cyclopropene alkenylamination. Chem Commun. https://doi.org/10.1039/d0cc01060j
64. Simaan M, Marek I (2018) Asymmetric catalytic preparation of polysubstituted cyclopropanol and cyclopropylamine derivatives. Angew Chem Int Ed. https://doi.org/10.1002/anie.201710707
65. Kwon Y, Wang Q (2020) Copper-catalyzed 1,2-aminocyanation of unactivated alkenes via cyano migration. Org Lett. https://doi.org/10.1021/acs.orglett.0c01217
66. Kwon Y, Zhang W, Wang Q (2021) Copper-catalyzed aminoheteroarylation of unactivated alkenes through distal heteroaryl migration. ACS Catal. https://doi.org/10.1021/acscatal.1c01001
67. Shen G, Zhao L, Wang Y, Zhang T (2016) Room temperature copper-catalyzed oxidative amidation of terminal alkynes for the synthesis of α-ketoamides using: *O*-benzoyl hydroxylamines as aminating reagent and oxidant. RSC Adv. https://doi.org/10.1039/c6ra15219h
68. Van Der Puyl VA, Derosa J, Engle KM (2019) Directed, nickel-catalyzed umpolung 1,2-carboamination of alkenyl carbonyl compounds. ACS Catal. https://doi.org/10.1021/acscatal.8b04516
69. Xie L, Wang S, Zhang L et al (2021) Directed nickel-catalyzed regio- and diastereoselective arylamination of unactivated alkenes. Nat Commun. https://doi.org/10.1038/s41467-021-26527-x

70. Brown HC, Heydkamp WR, Breuer E, Murphy WS (1964) The Reaction of organoboranes with chloramine and with hydroxylamine-O-sulfonic acid. A convenient synthesis of amines from olefins via hydroboration. J Am Chem Soc. https://doi.org/10.1021/ja01071a036
71. Brown HC, Kim KW, Srebnik M, Bakthan S (1987) Organoboranes for synthesis. 7. An improved general synthesis of primary amines from alkenes via hydroboration-organoborane chemistry. Tetrahedron. https://doi.org/10.1016/S0040-4020(01)83445-1
72. Rangaishenvi MV, Brown HC, Singaram B (1991) Chiral synthesis via organoboranes. 30. Facile synthesis, by the Matteson asymmetric homologation procedure, of α-methyl boronic acids not available from asymmetric hydroboration and their conversion into the corresponding aldehydes, ketones, carboxylic A. J Org Chem 20:25. https://doi.org/10.1021/jo00010a022
73. Matsuda N, Hirano K, Satoh T, Miura M (2012) Copper-catalyzed amination of arylboronates with *N,N*-dialkylhydroxylamines. Angew Chem 25:25. https://doi.org/10.1002/ange.201108773
74. Rucker RP, Whittaker AM, Dang H, Lalic G (2012) Synthesis of hindered anilines: copper-catalyzed electrophilic amination of aryl boronic esters. Angew Chem. https://doi.org/10.1002/ange.201200480
75. Rucker RP, Whittaker AM, Dang H, Lalic G (2012) Synthesis of tertiary alkyl amines from terminal alkenes: copper-catalyzed amination of alkyl boranes. J Am Chem Soc. https://doi.org/10.1021/ja3023829
76. Xiao Q, Tian L, Tan R et al (2012) Transition-metal-free electrophilic amination of arylboroxines. Org Lett. https://doi.org/10.1021/ol301912a
77. Mlynarski SN, Karns AS, Morken JP (2012) Direct stereospecific amination of alkyl and aryl pinacol boronates. J Am Chem Soc. https://doi.org/10.1021/ja305448w
78. Nishikawa D, Hirano K, Miura M (2016) Copper-catalyzed regio- and stereoselective aminoboration of alkenylboronates. Org Lett. https://doi.org/10.1021/acs.orglett.6b02338
79. Zhu H, Shen Y, Deng Q et al (2017) One-pot bimetallic Pd/Cu-catalyzed synthesis of sulfonamides from boronic acids, DABSO and *O*-benzoyl hydroxylamines. Chem Asian J 25:25. https://doi.org/10.1002/asia.201601732
80. Chen Y-H, Graßl S, Knochel P (2018) Cobalt-katalysierte elektrophile aminierung von aryl- und heteroarylzinkpivalaten mit N-hydroxylaminbenzoaten. Angew Chem. https://doi.org/10.1002/ange.201710931
81. Graßl S, Chen YH, Hamze C et al (2019) Late stage functionalization of secondary amines via a cobalt-catalyzed electrophilic amination of organozinc reagents. Org Lett. https://doi.org/10.1021/acs.orglett.8b03787
82. Yoon H, Kim Y, Lee Y (2017) Cu-Catalyzed electrophilic amination of internal alkynes via hydroalumination. Org Biomol Chem. https://doi.org/10.1039/c6ob02606k
83. Zhang Q, Hitoshio K, Saito H et al (2020) Copper-catalyzed electrophilic amination of alkoxyarylsilanes. Eur J Org Chem. https://doi.org/10.1002/ejoc.202000562
84. Lee S, Lee Y (2019) Copper-catalyzed electrophilic amination of benzoxazoles via magnesation. Eur J Org Chem. https://doi.org/10.1002/ejoc.201900335
85. Wang W, Peng X, Wei F et al (2016) Copper(I)-catalyzed interrupted click reaction: synthesis of diverse 5-hetero-functionalized triazoles. Angew Chem. https://doi.org/10.1002/ange.201509124
86. Hemric BN, Chen AW, Wang Q (2019) Copper-catalyzed modular amino oxygenation of alkenes: access to diverse 1,2-amino oxygen-containing skeletons. J Org Chem. https://doi.org/10.1021/acs.joc.8b02885
87. Yang Z, Jiang K, Chen YC, Wei Y (2019) Copper-catalyzed dihydroquinolinone synthesis from isocyanides and *O*-benzoyl hydroxylamines. J Org Chem. https://doi.org/10.1021/acs.joc.9b00262
88. Peterson LJ, Kirsch JK, Wolfe JP (2018) Pd-catalyzed alkene diamination reactions of nitrogen electrophiles: synthesis of cyclic guanidines and ureas bearing dialkylaminomethyl groups. Org Lett. https://doi.org/10.1021/acs.orglett.8b01289
89. Yu H, Li Z, Bolm C (2018) Copper-catalyzed transsulfinamidation of sulfinamides as a key step in the preparation of sulfonamides and sulfonimidamides. Angew Chem. https://doi.org/10.1002/ange.201810548
90. Zhu H, Shen Y, Deng Q et al (2017) Ligand-free Pd/Cu-catalyzed aminosulfonylation of aryl iodides for direct sulfonamide syntheses. Asian J Org Chem. https://doi.org/10.1002/ajoc.201700350
91. Zhang W, Wang C, Wang Q (2020) Copper-catalyzed decarboxylative functionalization of conjugated β, Γ-unsaturated carboxylic acids. ACS Catal 25:45. https://doi.org/10.1021/acscatal.0c03621

92. Dai Q, Zhang J (2018) Direct synthesis of sulfinamides by the copper-catalyzed electrophilic amidation of sulfenate anions. Adv Synth Catal. https://doi.org/10.1002/adsc.201701510
93. Nguyen VT, Haug GC, Nguyen VD et al (2021) Photocatalytic decarboxylative amidosulfonation enables direct transformation of carboxylic acids to sulfonamides. Chem Sci. https://doi.org/10.1039/d1sc01389k
94. Begam HM, Choudhury R, Behera A, Jana R (2019) Copper-catalyzed electrophilic ortho C(sp2)-H amination of aryl amines: dramatic reactivity of bicyclic system. Org Lett. https://doi.org/10.1021/acs.orglett.9b01546
95. Yao ZL, Wang L, Shao NQ et al (2019) Copper-catalyzed ortho-selective dearomative C–N coupling of simple phenols with *O*-benzoylhydroxylamines. ACS Catal. https://doi.org/10.1021/acscatal.9b01317
96. Li M, Wang DH (2021) Copper-catalyzed 3-positional amination of 2-azulenols with *O*-benzoylhydroxylamines. Org Lett. https://doi.org/10.1021/acs.orglett.1c02132
97. Rao WH, Li Q, Jiang LL et al (2021) Copper-catalyzed intermolecular C(sp2)-H amination with electrophilic *O*-benzoyl hydroxylamines. J Org Chem. https://doi.org/10.1021/acs.joc.1c01229
98. Catellani M, Frignani F, Rangoni A (1997) A complex catalytic cycle leading to a regioselective synthesis of O, O-disubstituted vinylarenes. Angew Chem (Int Ed English). https://doi.org/10.1002/anie.199701191
99. Motti E, Ippomei G, Deledda S, Catellani M (2003) Synthesis of selectively substituted ortho-vinylbiphenyls by palladium-catalysed reaction of ortho-substituted aryl iodides with olefins. Synthesis (Stuttg). https://doi.org/10.1055/s-2003-42441
100. Martins A, Mariampillai B, Lautens M (2010) Synthesis in the key of Catellani: norbornene-mediated ortho C–H functionalization. Top Curr Chem 25:25
101. Ferraccioli R (2013) Palladium-catalyzed synthesis of carbo- and heterocycles through norbornene-mediated ortho C–H functionalization. Synth. https://doi.org/10.1055/s-0032-1318218
102. Ye J, Lautens M (2015) Palladium-catalysed norbornene-mediated C-H functionalization of arenes. Nat Chem 20:25
103. Della Ca N, Fontana M, Motti E, Catellani M (2016) Pd/norbornene: a winning combination for selective aromatic functionalization via C–H bond activation. Acc Chem Res. https://doi.org/10.1021/acs.accounts.6b00165
104. Dong Z, Dong G (2013) Ortho vs ipso: site-selective pd and norbornene-catalyzed arene C–H amination using aryl halides. J Am Chem Soc. https://doi.org/10.1021/ja410823e
105. Chen ZY, Ye CQ, Zhu H et al (2014) Palladium/norbornene-mediated tandem C–H amination/C-I alkenylation reaction of aryl iodides with secondary cyclic *O*-benzoyl hydroxylamines and activated terminal olefins. Chem A Eur J. https://doi.org/10.1002/chem.201400084
106. Ye C, Zhu H, Chen Z (2014) Synthesis of biaryl tertiary amines through Pd/norbornene joint catalysis in a remote C–H amination/Suzuki coupling reaction. J Org Chem. https://doi.org/10.1021/jo501544h
107. Zhou PX, Ye YY, Ma JW et al (2014) Palladium-catalyzed/norbornene-mediated ortho-amination/N-tosylhydrazone insertion reaction: an approach to the synthesis of ortho-aminated vinylarenes. J Org Chem. https://doi.org/10.1021/jo501125b
108. Pan S, Ma X, Zhong D et al (2015) Palladium-catalyzed one-pot consecutive amination and Sonogashira coupling for selective synthesis of 2-alkynylanilines. Adv Synth Catal. https://doi.org/10.1002/adsc.201500381
109. Shi H, Babinski DJ, Ritter T (2015) Modular C–H functionalization cascade of aryl iodides. J Am Chem Soc. https://doi.org/10.1021/jacs.5b01082
110. Sun F, Gu Z (2015) Decarboxylative alkynyl termination of palladium-catalyzed Catellani reaction: a facile synthesis of α-alkynyl anilines via ortho C–H amination and alkynylation. Org Lett. https://doi.org/10.1021/acs.orglett.5b00830
111. Wang J, Gu Z (2016) Synthesis of 2-(1-alkoxyvinyl)anilines by palladium/norbornene-catalyzed amination followed by termination with vinyl ethers. Adv Synth Catal. https://doi.org/10.1002/adsc.201600339
112. Majhi B, Ranu BC (2016) Palladium-catalyzed norbornene-mediated tandem ortho-C–H-amination/ipso-C-I-cyanation of iodoarenes: regiospecific synthesis of 2-aminobenzonitrile. Org Lett. https://doi.org/10.1021/acs.orglett.6b02113
113. Luo B, Gao JM, Lautens M (2016) Palladium-catalyzed norbornene-mediated tandem amination/cyanation reaction: a method for the synthesis of ortho-aminated benzonitriles. Org Lett. https://doi.org/10.1021/acs.orglett.6b02249

114. Whyte A, Olson ME, Lautens M (2018) Palladium-catalyzed, norbornene-mediated, ortho-amination ipso-amidation: sequential C–N bond formation. Org Lett. https://doi.org/10.1021/acs.orglett.7b03577
115. Fan L, Liu J, Bai L et al (2017) Rapid assembly of diversely functionalized spiroindenes by a three-component palladium-catalyzed C−H amination/phenol dearomatization domino reaction. Angew Chem. https://doi.org/10.1002/ange.201708310
116. Wang J, Li R, Dong Z et al (2018) Complementary site-selectivity in arene functionalization enabled by overcoming the ortho constraint in palladium/norbornene catalysis. Nat Chem. https://doi.org/10.1038/s41557-018-0074-z
117. Dong Z, Lu G, Wang J et al (2018) Modular ipso/ortho difunctionalization of aryl bromides via palladium/norbornene cooperative catalysis. J Am Chem Soc. https://doi.org/10.1021/jacs.8b04153
118. Zhang BS, Li Y, An Y et al (2018) Carboxylate ligand-exchanged amination/C(sp3)-H arylation reaction via Pd/norbornene cooperative catalysis. ACS Catal. https://doi.org/10.1021/acscatal.8b04163
119. Chen S, Wang P, Cheng HG et al (2019) Redox-neutral: ortho -C–H amination of pinacol arylborates via palladium(ii)/norbornene catalysis for aniline synthesis. Chem Sci. https://doi.org/10.1039/c9sc02759a
120. Abel-Snape X, Whyte A, Lautens M (2020) Synthesis of aminated phenanthridinones via palladium/norbornene catalysis. Org Lett. https://doi.org/10.1021/acs.orglett.0c02850
121. An Y, Zhang BS, Zhang Z et al (2020) A carboxylate-assisted amination/unactivated C(sp2)-H arylation reaction via palladium/norbornene cooperative catalysis. Chem Commun 25:5
122. Chen Y, Lv W, Ba D et al (2020) Palladium-catalyzed chemoselective synthesis of 2-aminocinnamyl esters via sequential amination and olefination of aryl iodides. J Org Chem. https://doi.org/10.1021/acs.joc.0c01695
123. Zhang BS, Li Y, Gou XY et al (2020) DMAP and PivOH-promoted amination/allenization reaction. Chem Commun. https://doi.org/10.1039/d0cc03749d
124. Wang CT, Li M, Ding YN et al (2021) Alkylation-terminated Catellani reactions by cyclobutanol C-C cleavage. Org Lett. https://doi.org/10.1021/acs.orglett.0c04018
125. Zhao S, Han S, Du G et al (2021) Acid-promoted expeditious syntheses of aminated dibenzosultams via palladium/norbornene cooperatively catalysed C−H amination/arylation. Adv Synth Catal. https://doi.org/10.1002/adsc.202001413
126. Zheng N, Liu C, Ding YN et al (2020) Copper-catalyzed three-component redox-neutral ring opening of benzothiazoles to 1-amino-N-(2-(phenylthio)phenyl)methanimine. J Org Chem. https://doi.org/10.1021/acs.joc.9b03489