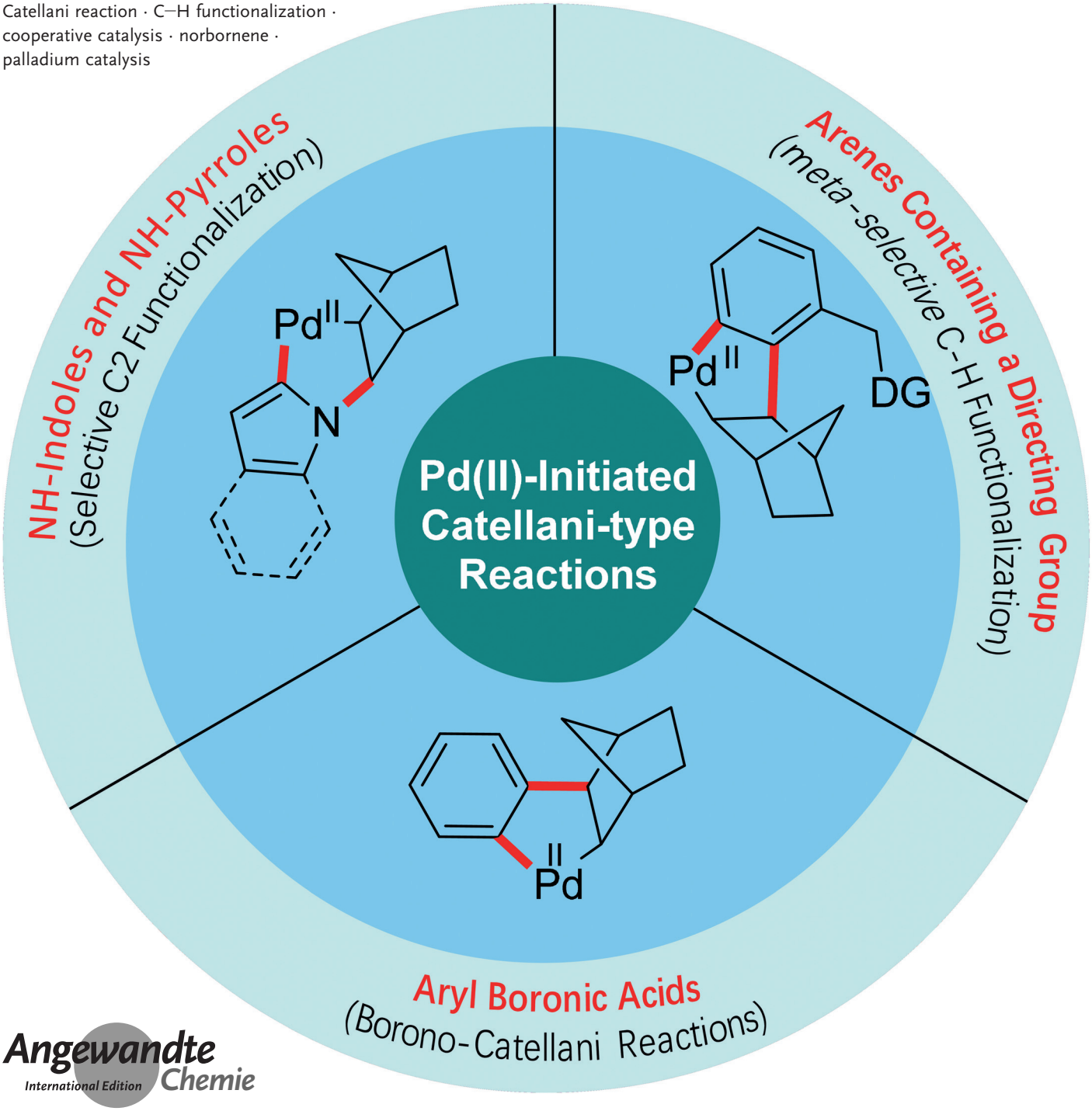
C–H Functionalization

International Edition: DOI: 10.1002/anie.201813491
German Edition: DOI: 10.1002/ange.201813491

Palladium(II)-Initiated Catellani-Type Reactions

*Hong-Gang Cheng, Shuqing Chen, Ruiming Chen, and Qianghui Zhou**

Keywords:
Catellani reaction · C–H functionalization · cooperative catalysis · norbornene · palladium catalysis



The Catellani reaction is known as a powerful strategy for the expeditious synthesis of highly substituted arenes and benzo-fused rings, which are usually difficult to access through traditional cross-coupling strategies. It utilizes the synergistic interplay of palladium and norbornene catalysis to facilitate sequential ortho C–H functionalization and ipso termination of aryl halides in a single operation. In classical Catellani-type reactions, aryl halides are mainly used as the substrates, and a Pd^0 catalyst is required to initiate the reaction. Nevertheless, recent advances showcase that Catellani-type reactions can also be initiated by a Pd^{II} catalyst with different starting materials instead of aryl halides via different reaction mechanisms and under different conditions. This emerging concept of Pd^{II}/norbornene cooperative catalysis has significantly advanced Catellani-type reactions, thus enabling future developments of this field. In this Minireview, Pd^{II}-initiated Catellani-type reactions and their application in the synthesis of bioactive molecules are summarized.

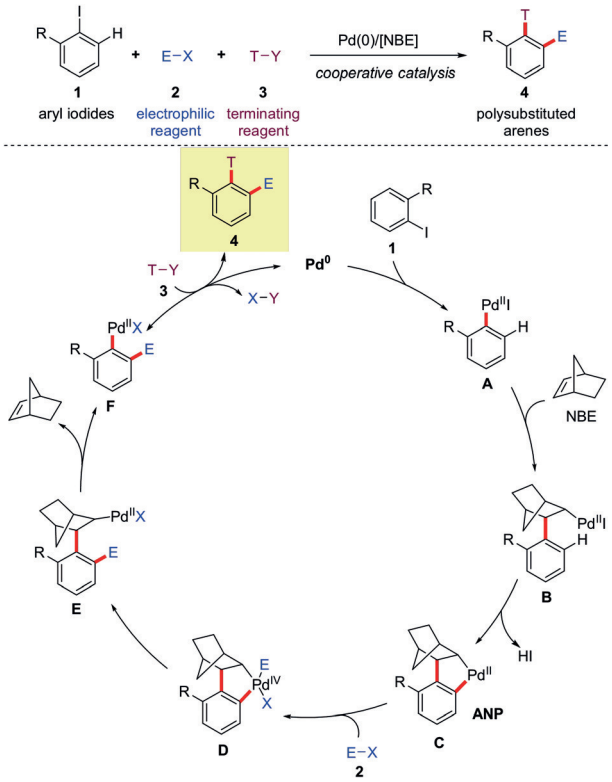
1. Introduction

The selective, modular, and efficient assembly of molecular complexity represents one of the most challenging yet fascinating directions in modern synthetic organic chemistry.[1] Therein, the transition-metal-catalyzed C–H functionalization of arenes is among the most attractive strategies.[2] As it can be used to construct carbon–carbon or carbon–heteroatom bonds in a direct and selective manner, various game-changing disconnection strategies for organic synthesis have thus been provided. Over decades, this field has attracted much attention from both academic and industrial laboratories.

In this context, Pd/norbornene (NBE) cooperative catalysis, namely the Catellani reaction, is one of the most promising approaches. It utilizes the synergistic interplay of palladium and NBE catalysis to facilitate sequential *ortho* C–H functionalization and *ipso* termination of aryl halides. Since the pioneering work by the groups of Catellani[3] and Lautens,[4] this chemistry has attracted considerable attention from the organic synthesis community. Over more than twenty years of development, it has become a powerful strategy for the expeditious synthesis of highly substituted arenes, which are difficult to access through traditional cross-coupling reactions.[5]

As shown in Scheme 1, in traditional Catellani-type reactions, aryl halides (mainly aryl iodides) are used as the substrates, and a Pd^0 catalyst is required to generate the arylpalladium(II) species **A**, which can undergo carbopalladation with NBE to form intermediate **B**. A subsequent *ortho* C–H activation leads to the formation of the key aryl norbornylpalladacycle **C** (ANP). Then, oxidative addition of an electrophile **2** (E-X) to **C** generates Pd^{IV} species **D**, which delivers norbornylpalladium(II) species **E** upon reductive elimination. If the R group is a hydrogen atom, a second *ortho* C–H activation will occur, following the same procedure. Otherwise, because of increased steric interactions between the palladium center and the two *ortho* substituents, in addition to the lack of a β-hydrogen atom *syn* to palladium in intermediate **E**, a retro-carbopalladation to regenerate NBE will take place to provide arylpalladium(II) species **F**, which undergoes a traditional cross-coupling reaction with the terminating reagent **3** (T-Y) to afford the polysubstituted arene **4** and regenerate the Pd^0 species catalyst.[6]

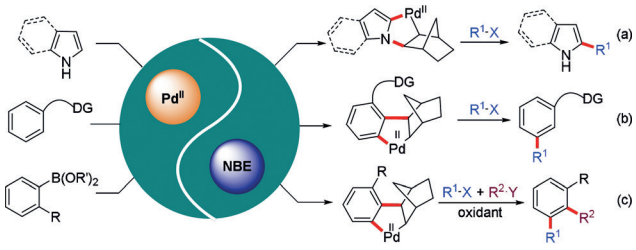
According to the above proposed mechanism, it can be surmised that this kind of reaction may also be initiated by a Pd^{II} catalyst to form the common arylpalladium(II) species from suitable starting materials that are different from aryl halides. Indeed, owing to the efforts of Bach, Yu, and others, a suite of elegant Pd^{II}-initiated Catellani-type reactions have



Scheme 1. Traditional Pd^0-initiated Catellani-type reaction and suggested mechanism.

[*] Dr. H.-G. Cheng, S. Chen, R. Chen, Prof. Dr. Q. Zhou
College of Chemistry and Molecular Sciences
Institute for Advanced Studies (IAS), Wuhan University
430072 Wuhan (P. R. China)
E-mail: qhzhou@whu.edu.cn
Homepage: http://qhzhou.whu.edu.cn
The ORCID identification number(s) for the author(s) of this article can be found under:
https://doi.org/10.1002/anie.201813491.

been developed in the past few years (Scheme 2). Different from the conventional Catellani reaction, this Pd^{II}/NBE cooperative catalysis proceeds with completely different substrates and a different reaction mechanism, and thus the



Scheme 2. Pd^{II}-initiated Catellani-type reactions: a) C2 functionalization of NH-indoles and NH-pyrroles. b) *meta*-Selective C–H functionalization of arenes. c) Borono-Catellani reactions. DG = directing group.

reaction conditions are significantly different or even orthogonal. This emerging concept of Pd^{II}/NBE cooperative catalysis has tremendously advanced Catellani-type reactions, therefore opening a new avenue for future developments in this field. Although there have been several elegant reviews and accounts published for Pd/NBE cooperative catalysis,[5] one focusing on these emerging Pd^{II}-initiated Catellani-type reactions are still lacking yet highly desired. In this context, we have comprehensively summarized the recent advances and breakthroughs in this direction in this Minireview, hoping to inspire future studies and promote new developments in this field. This Minireview was divided into Sections according to the type of substrate interacting with the Pd^{II} catalyst, including NH-indoles and NH-pyrroles, arenes with a directing group, as well as aryl boronic acids and their derivatives.

2. C2 Functionalization of NH-Indoles and NH-Pyrroles

Indoles and pyrroles are two important classes of heterocycles. Although considerable efforts have been made in the direct C–H functionalization of indoles and pyrroles, the regioselective C2 functionalization of these heterocycles remains a challenge.

Recently, a direct C2 functionalization (mainly alkylation and arylation) of NH-indoles and NH-pyrroles was realized by Pd^{II}/NBE cooperative catalysis. The Bach group initiated this research and made major contributions.[5j] In this Section, we have summarized the C2 functionalization of NH-indoles and NH-pyrroles by Pd^{II}/NBE cooperative catalysis. The contents discussed have been catalogued according to the functionalization reagents employed.

2.1. C2 Alkylation of NH-Indoles

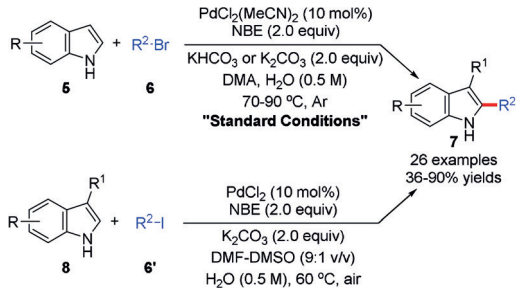
Studies in this direction were initiated by Bach and coworkers in 2011, who developed reactions between NH-indoles and primary alkyl halides (bromides or iodides) that selectively generate C2-alkylated indoles under cooperative Pd^{II}/NBE catalysis (Scheme 3).[7,8] By making use of this facile transformation, an array of structurally diverse 2-alkylindoles were synthesized in moderate to excellent yields.

Dr. Hong-Gang Cheng was born in Jiangxi Province, China, and received his Ph.D. degree under the supervision of Prof. Wen-Jing Xiao from Central China Normal University in 2014. He then joined Prof. Shū Kobayashi's group as a Postdoctoral Fellow at the University of Tokyo and worked there for one year. He is currently a Research Associate in Prof. Qianghui Zhou's group at Wuhan University. His research interests include the development of new synthetic methodologies and total synthesis of bioactive natural products.

Shuqing Chen was born in Hunan Province, China, and received his B.Sc. degree from Xiangtan University in 2014. Since earning his M.Sc. degree from Xiangtan University under the direction of Prof. Guojun Deng and Assoc. Prof. Fuhong Xiao in 2017, he has been pursuing his Ph.D. degree under the guidance of Prof. Qianghui Zhou at Wuhan University. His research interests focus on synthetic methodology development and asymmetric catalysis.

Ruiming Chen was born in Fujian Province, China, and received his B.Sc. degree from Wuhan University in 2018. He then pursued his graduate studies at the same university under the direction of Prof. Qianghui Zhou. His research interests focus on synthetic methodology development and the total synthesis of natural products.

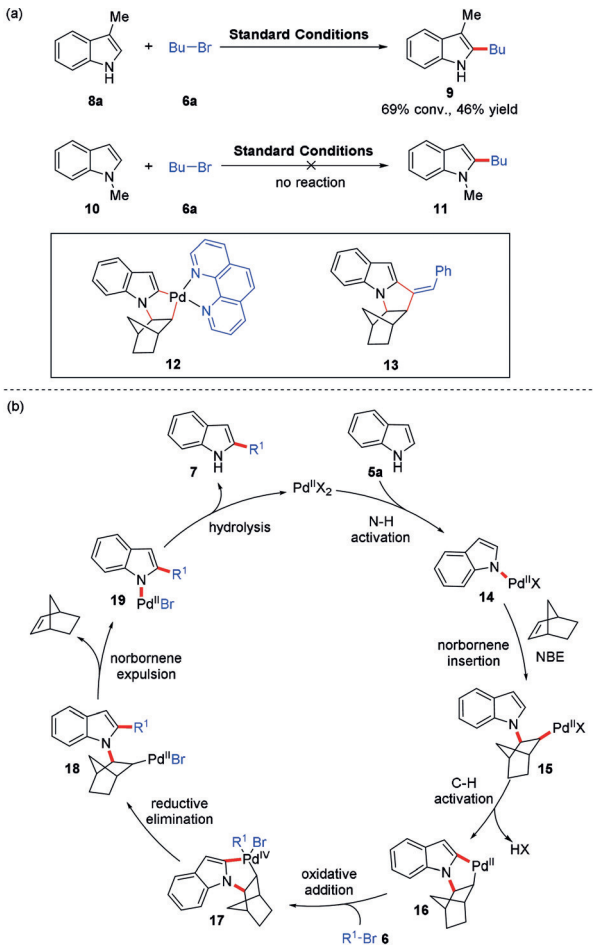
Prof. Dr. Qianghui Zhou received his B.S. from Peking University in 2005. He pursued graduate studies under the guidance of Prof. Dawei Ma at Shanghai Institute of Organic Chemistry and earned his Ph.D. degree in 2010. He then took a postdoctoral position in the lab of Prof. Phil S. Baran at the Scripps Research Institute. In June 2015, he began his independent career at the College of Chemistry and Molecular Sciences of Wuhan University. His group currently focuses on developing novel methodologies for the synthesis of biologically important molecules.



Scheme 3. Selective C2 alkylation of NH-indoles. DMA = *N*,*N*-dimethylacetamide, DMF = *N*,*N*-dimethylformamide.

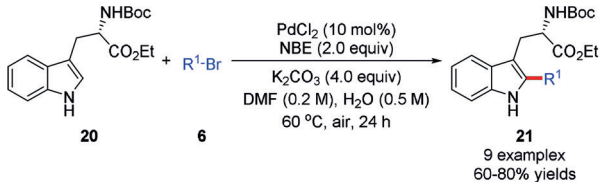
For 3-substituted NH-indoles, a modified procedure was required, involving more reactive alkyl iodide reagents, a more polar solvent, and air atmosphere (Scheme 3). For electron-deficient NH-indoles, a weaker base such as $KHCO_3$ or K_2HPO_4 was required so as to prevent direct N-alkylation of the indoles. Lastly, it was found that the addition of water dramatically accelerated this process.

Mechanistic studies showed that 3-substituted NH-indoles were suitable substrates whereas N-substituted indoles exhibited no reactivity at all, indicating the pivotal role of the free NH moiety (Scheme 4a). Moreover, through careful reaction design, key complex **12** and trapping product **13** were isolated and characterized (Scheme 4a). Based on these results, a reaction mechanism was put forward (Scheme 4b). Initially, the free N–H bond of indole **5** is activated by Pd^{II}, which is followed by NBE insertion to form complex **15**. Cyclopalladation of **15** generates the five-membered palladacycle **16**. Then, oxidative addition of alkyl bromide to **16** gives the Pd^{IV} complex **17**, which undergoes reductive elimination to deliver norbornylpalladium(II) intermediate **18**. Lastly, NBE expulsion from **18** followed by protolysis of the resulting intermediate **19** affords the final product, 2-alkylindole **7**, and regenerates the Pd^{II} catalyst.[8]



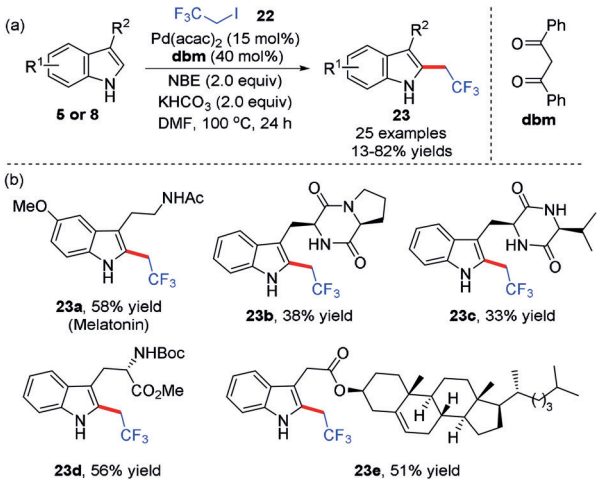
Scheme 4. a) Control experiments and isolated intermediates. b) Proposed catalytic cycle for the Pd^{II}/NBE-catalyzed C2 alkylation of NH-indoles.

A number of C2-alkylated tryptophan derivatives **21** were prepared in good yields in a similar process from the N-Boc-protected ethyl ester of (*S*)-tryptophan (**20**). Significantly, the reaction proceeded without any loss of the enantiomeric purity inherited from the chiral tryptophan substrate (Scheme 5).[9] It should be noted that this transformation requires air to proceed to prevent reduction of Pd^{II} to Pd^0, just as for the previously mentioned C3-substituted indole substrates.



Scheme 5. C2 alkylation of an NH-tryptophan derivative.

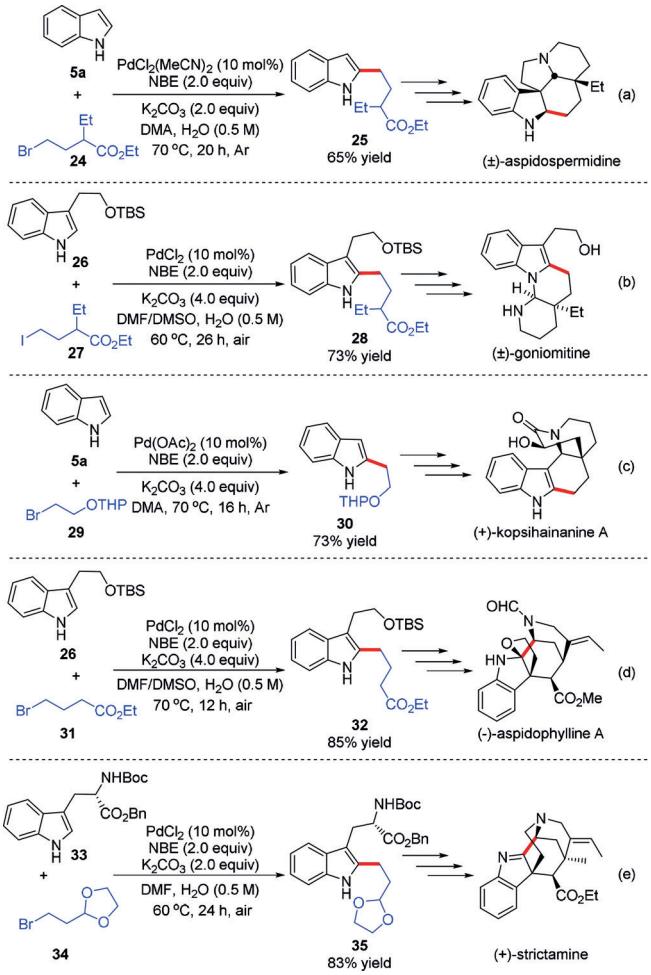
Recently, Liu[10] and co-workers utilized this strategy for the selective C2 trifluoroethylation of indoles with commercially available trifluoroethyl iodide as the alkylating reagent (Scheme 6a). The reaction displays a wide functional group tolerance, and can even be utilized for the late-stage trifluoroethylation of complex indole derivatives (Scheme 6b). Preliminary mechanistic studies show that the unique



Scheme 6. C2 trifluoroethylation of NH-indoles. acac = acetylacetonate, dbm = dibenzoylmethane.

anionic ligand dibenzoylmethane (dbm) plays a critical role in governing the efficiency of this transformation by accelerating the oxidative addition step of the unreactive trifluoroethyl iodide to the ANP intermediate **16**. In addition, DFT calculations suggested that the N–H activation of the indole substrate is involved in the rate-determining step.

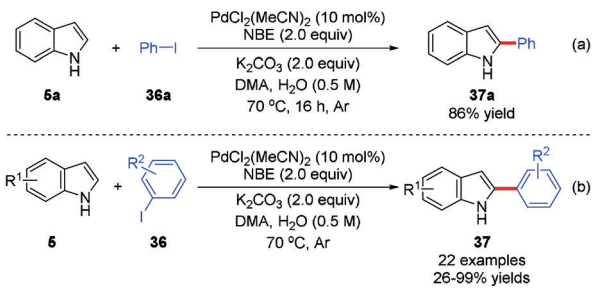
Remarkably, the synthetic utility of this selective C2 alkylation strategy of indoles was demonstrated by its application in the efficient synthesis of several complex indole alkaloids, such as (±)-aspidospermidine (Scheme 7a),[8a] (±)-goniomitine (Scheme 7b),[8a] (+)-kopsihainanine A (Scheme 7c),[11] (−)-aspidophylline A (Scheme 7d),[12] and (+)-strictamine (Scheme 7e).[13]



Scheme 7. Application of the Pd^{II}/NBE-catalyzed C2 alkylation of NH-indoles as one of the key steps in the total synthesis of complex indole alkaloids.

2.2. C2 Arylation of NH-Indoles

Based on the success of the selective C2 alkylation of NH-indoles through Pd^{II}/NBE cooperative catalysis, the Bach group demonstrated that this chemistry could be extended to C2 arylation by selecting iodobenzene as the coupling partner. However, only one such example was presented in their report in 2011 (Scheme 8a).[7] Recently, the groups of

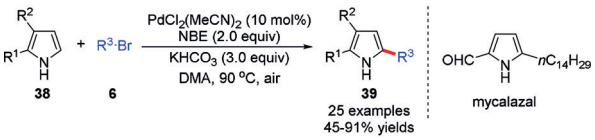


Scheme 8. C2 arylation of NH-indoles.

Xue and Jiang intensively explored this topic, and successfully synthesized a variety of C2-arylated NH-indoles in moderate to excellent yields (Scheme 8b).[14] It was found that a combination of electron-rich indoles and electron-poor aryl iodides usually led to good results, probably because the corresponding *ortho* C–H activation and oxidative addition steps are facilitate.

2.3. C2 Alkylation of NH-Pyrroles

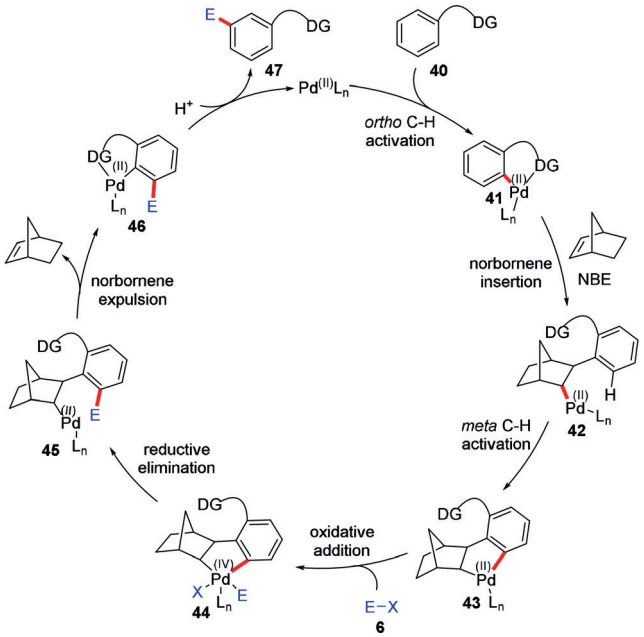
Aside from indole substrates, Bach and co-workers applied the Pd^{II}/NBE cooperative catalysis chemistry to NH-pyrroles for selective C2 alkylation, which used to be a very challenging task. As pyrroles are more electron-rich and less acidic than indoles, initial attempts with such pyrroles, for example, 2-phenylpyrrole, were unsuccessful. However, electron-deficient pyrroles are suitable substrates for this transformation, delivering the corresponding alkylated pyrroles **39** in moderate to excellent yields.[15] Utilizing this reaction as the key step, a short synthesis of the lipophilic pyrrole natural product mycalazal was realized (Scheme 9).



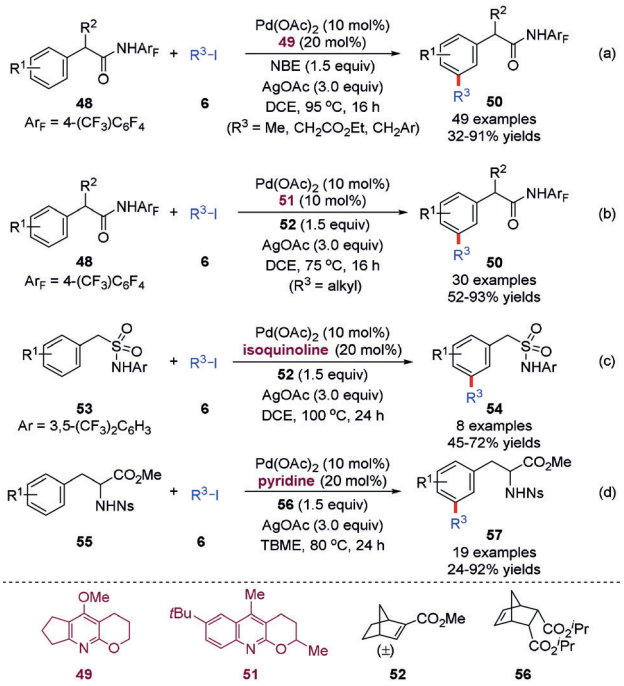
Scheme 9. C2 alkylation of NH-pyrroles.

3. meta-Selective C–H Functionalization of Arenes

Transition-metal-catalyzed site-selective C–H functionalization has continuously been a highly impactful process in synthetic chemistry.[16] Whereas *ortho*-selective C–H functionalization reactions of arenes have been well developed, *meta*-selective C–H functionalization remains a challenge. Recently, several elegant strategies have been developed to address this issue,[16g,i,17–19] for example, steric-hindrance-sensitive borylation,[17] ruthenium-catalyzed *meta*-selective C–H functionalization,[18] and the use of a U-shaped template.[19] A separate approach using Pd^{II}/NBE cooperative catalysis was developed by the groups of Yu, Dong, Zhao, Shi, Ferreira, and others,[20–37] who drew inspiration from the Catellani reaction. As shown in Scheme 10, by taking advantage of the directed *ortho* palladation and Catellani's



Scheme 10. Proposed catalytic cycle of the Pd^{II}/NBE-co-catalyzed *meta* C–H functionalization.



Scheme 11. *meta*-Selective C–H alkylations.

NBE-mediated insertion/deinsertion, functionalization at the *meta* position of the arene substrate can be readily achieved. It should be pointed out that in these *meta*-selective C–H functionalization processes, stoichiometric silver salts are usually needed, which may act as a base for the C–H activation steps, as an oxidant to prevent the formation of Pd^0 species, as well as a halogen anion scavenger to promote the formation of Pd^{IV} species. Further studies illustrated the use of this strategy in generating derivatives of phenylacetic acid, β-arylethylamines, benzyl amines, anilines, and phenols.

In this Section, we have summarized the *meta*-selective C–H functionalization of arenes by Pd^{II}/NBE cooperative catalysis. The contents are ordered according to the type of functionalization, including alkylation, arylation, chlorination, amination, and alkynylation. Enantioselective *meta* C–H functionalization co-catalyzed by a chiral NBE-type mediator and Pd^{II} will be discussed separately.

3.1. meta-*Selective C–H Alkylation*

Inspired by the unique Pd^0-initiated Catellani-type reactions of aryl iodides and in line with their continuous interest in directed C–H functionalization, Yu and co-workers developed an elegant approach for the *meta* C–H alkylation of phenylacetic amides by Pd^{II}/NBE cooperative catalysis in 2015 (Scheme 11 a).[20] This transformation provided the first proof of concept that *meta* C–H alkylation can be achieved through directed *ortho* C–H activation followed by involvement of NBE as a mediator. The use of a newly developed pyridine-based ligand **49** proved crucial for relaying the palladium catalyst to the *meta* position by NBE after the initial *ortho*-C–H activation. Nevertheless, this process suffered from a narrow substrate scope as the alkylating reagent was limited to those without β-hydrogen atoms, for example, iodomethane, ethyl iodoacetate, and benzyl halides.

To overcome the aforementioned limitation, the same group introduced a more reactive mediator, 2-carbomethoxynorbornene (**52**; Yu mediator), in combination with the quinoline-type ligand **51** to successfully develop a more general and efficient *meta* C–H alkylation process with a broader scope of alkylating reagents (13 examples; Scheme 11 b).[21]

Later on, they realized the *meta* C–H alkylation of benzylsulfonamide (sulfonamide as an *ortho*-directing group) by using Yu mediator **52** and simple isoquinoline as the ligand, generating the desired *meta*-alkylated products **54** in 45–72 % yield (Scheme 11 c).[22]

Very recently, Ding and co-workers reported the direct *meta* alkylation of nosyl-protected methyl esters of phenylalanine derivatives in moderate to high yields (Scheme 11 d).[23] In this process, another NBE derivative, diisopropyl bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**56**), was introduced together with simple pyridine as the optimal combination of mediator and ligand. Significantly, no racemization occurred in this transformation.

It should be pointed out that in the *meta*-selective C–H alkylation processes described above, hindered secondary alkyl iodides and bromides were all demonstrated to be unsuitable alkylating reagents.

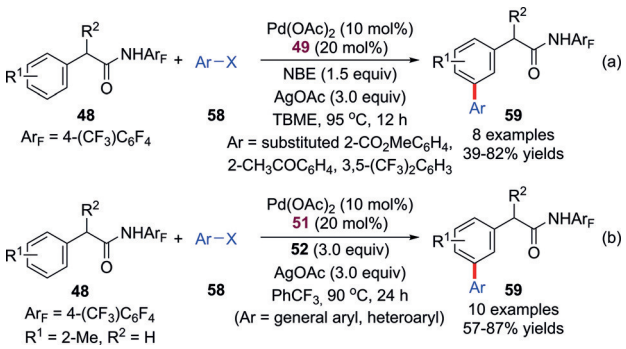
3.2. meta-*Selective C–H Arylation*

Biaryl motifs are ubiquitous in bioactive natural products and pharmaceuticals.[24] Consequently, extensive efforts have been devoted to the development of efficient methods to assemble biaryls in a rapid fashion. Following the success of

meta C–H alkylation reactions of arenes by Pd^{II}/NBE cooperative catalysis, the groups of Yu and others demonstrated that this strategy could be extended to *meta* C–H arylation, thus providing a unique access to diversified biaryls. To present these achievements in an easy-to-follow way, the contents will be discussed separately according to the type of applied *ortho* directing group, which include amide, sulfonamide, tertiary amine, pyridine, quinoline, and free carboxylic acid, groups.

3.2.1. Amides or Sulfonamides as Directing Groups

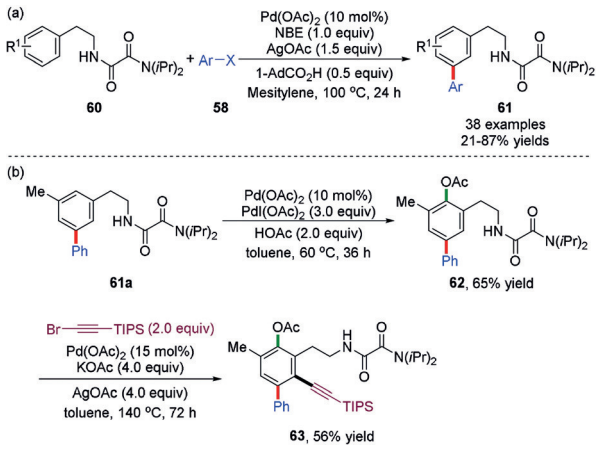
Following the success of *meta* C–H alkylation of phenylacetic amides by Pd^{II}/NBE cooperative catalysis in 2015, Yu and co-workers reported the corresponding selective *meta* C–H arylation (Scheme 12a).[20] Under slightly modified reaction conditions compared to Scheme 11a, a series of aryl iodides with *ortho*-coordinating groups as well as highly reactive 3,5-bis(trifluoromethyl)iodobenzene were found to be competent coupling partners, providing the corresponding biaryls **59** in moderate to high yields.



Scheme 12. *meta*-Selective C–H arylations of phenylacetic amides.

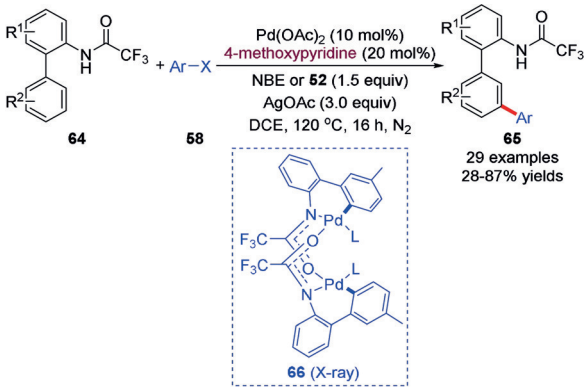
Despite these advances, the arylating reagents involved in the above reaction were mainly limited to aryl iodides with electron-withdrawing *ortho*-coordinating groups or multiple electron-withdrawing substituents. Therefore, the development of a more general *meta* arylation procedure compatible with common aryl iodides was highly desirable. To this end, Yu and co-workers developed an efficient *meta*-selective C–H arylation process with a broader scope of aryl iodides, which was realized with the aid of quinoline ligand **51** and Yu mediator **52** (Scheme 12b).[21]

In 2016, Zhao and co-workers reported a selective *meta* arylation of β-arylethylamine derivatives **60** with a bidentate oxalyl-amide-based directing group and simple NBE as the mediator (Scheme 13).[25a] A variety of aryl iodides bearing *ortho*, *meta*, or *para* substituents reacted well to provide the desired biaryls in moderate to high yields. Notably, the obtained products were further elaborated through sequential *ortho* C–H functionalizations to afford the polysubstituted arylethylamine derivative **63** in moderate yield (Scheme 13b).[25b]



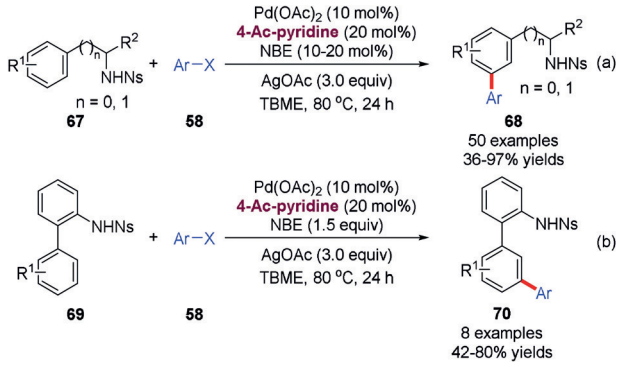
Scheme 13. *meta*-Selective C–H arylation of β-arylethylamine derivatives.

Later, Shi and co-workers developed a selective interannular *meta* C–H arylation of biaryl-2-trifluoroacetamides (Scheme 14).[26] In this process, the trifluoroacetyl protecting group is crucial for the interannular selectivity, which may due to its electronic properties and binding ability. It was noted that the reaction proceeded well with aryl iodides bearing an *ortho* electron-withdrawing group. In contrast, aryl iodides with *meta* or *para* substituents gave the corresponding products in particularly low yields. In these cases, switching from NBE to Yu mediator **52** improved the reaction yields. Remarkably, the authors unambiguously determined that the dimeric palladacycle **66**, comprising two cyclopalladated trifluoroacetamino biaryl units linked through trifluoroacetamide, was the key intermediate of this transformation.



Scheme 14. *meta*-Selective C–H arylation of biaryl-2-trifluoroacetamides.

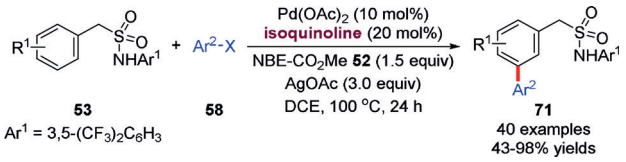
In 2017, Yu and co-workers reported a Pd^{II}/NBE cooperatively catalyzed *meta*-selective C–H arylation of nosyl-protected arylethylamines and phenylglycine esters **67**, wherein the common sulfonamide was used as the directing group (Scheme 15a).[27] Subjecting nosyl-protected 2-aryl anilines **69** to this process led to *meta* C–H arylation at the remote aryl ring (Scheme 15b). Addition of 4-acetylpyridine as the ligand was key to this process, and the palladium



Scheme 15. *meta*-Selective C–H arylation of nosyl-protected aryl ethylamines, phenylglycines, and 2-aryl anilines.

catalyst loading could be reduced to as low as 2.5 mol%. This catalytic system is compatible with various aryl iodides as well as aryl bromides with *ortho*-coordinating groups, giving the corresponding biaryls in moderate to high yields. It should be mentioned that in the case of nosyl-protected arylethylamines **67**, a catalytic amount of NBE (10–20 mol%) was sufficient to mediate this *meta* C–H arylation reaction efficiently, which represented the first example in this field (Scheme 15a).

Utilizing a sulfonamide as the directing group for the *meta*-selective C–H arylation of benzylsulfonamide derivatives **53** through Pd^{II}/NBE cooperative catalysis was also recently reported by the Yu group (Scheme 16).[22] The reaction was carried out by using isoquinoline as the ligand

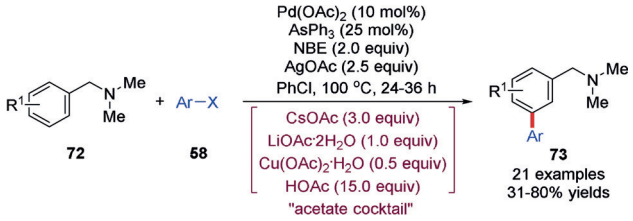


Scheme 16. *meta*-Selective C–H arylation of benzyl sulfonamides.

and **52** as the mediator, enabling facile syntheses of *meta*-arylated benzylsulfonamide derivatives **71**. Importantly, the obtained products can be readily transformed into sodium sulfonates, sulfonate esters, sulfonamides, as well as styrenes by Julia-type olefination.

3.2.2. Tertiary Amines as Directing Groups

In 2015, Dong and co-workers reported a distinct *meta* arylation of arenes by Pd^{II}/NBE catalysis, using a tertiary amine as the directing group (Scheme 17).[28] It was worth noting that the reaction was promoted by $AsPh_3$ as the ligand and an interesting "acetate cocktail" containing LiOAc·$2H_2O$, CsOAc, $Cu(OAc)_2·H_2O$, and acetic acid. A wide range of functional groups, including some heteroarenes, were tolerated under the reaction conditions. However, an *ortho* electron-withdrawing substituent on the aryl iodide was required to render it a suitable coupling partner. Moreover,

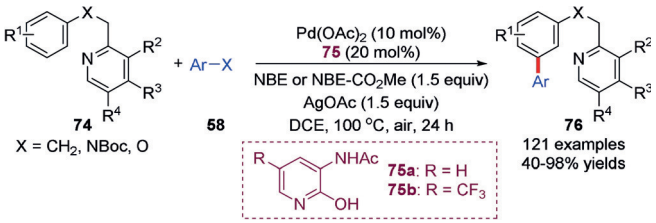


Scheme 17. *meta*-Selective C–H arylation of benzyl amines.

the amine directing group can be easily transformed into other common functional groups.

3.2.3. Tethered Pyridine-type Directing Groups

In 2016, *meta*-selective C–H arylation reactions of anilines, heteroaromatic amines, phenols, and 2-benzylpyridine derivatives **74** were realized by the Yu group (Scheme 18).[29]

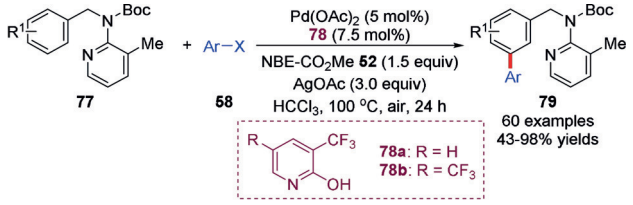


Scheme 18. *meta*-Selective C–H arylation of aniline, heterocyclic aromatic amine, phenol, and 2-benzyl heterocycle derivatives.

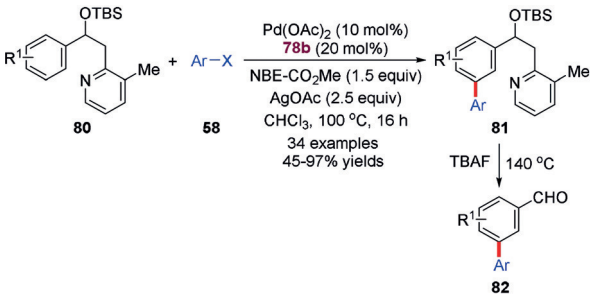
By using the versatile 3-acetylamino-2-hydroxypyridine **75a** or its trifluoromethylated derivative **75b** as the ligand and NBE as the mediator, a large number of *meta*-arylated products **76** were afforded in good to excellent yields. This process also exhibited good compatibility with both heteroarene substrates and heteroaryl halide coupling partners. The utility of this method in drug discovery was showcased through the late-stage *meta* C–H arylation of a lenalidomide derivative in good yield.

Later on, the same group developed an elegant *meta*-selective C–H arylation of benzylamines with a pyridine-type N-substituted directing group. The reaction was promoted by Yu mediator **52** and pyridone-type ligand **78**, and the corresponding *meta*-arylated benzylamine derivatives **79** were obtained in moderate to excellent yields (Scheme 19).[30]

Very recently, the same group achieved the *meta* C–H arylation of masked aromatic aldehydes **80** by employing Yu mediator **52** and pyridone-type ligand **78b** (Scheme 20).[31]



Scheme 19. *meta*-Selective C–H arylation of benzylamine derivatives.

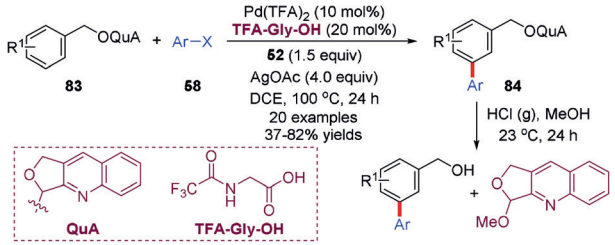


Scheme 20. *meta*-Selective C–H arylation of masked aromatic aldehydes.

The process relied on a pyridine-type directing group, which also served as a masking group for aryl aldehydes, and was readily installed and removed. Control experiments indicated that the correct length of this directing group was crucial for permitting the critical migratory insertion step to proceed efficiently. A wide variety of masked aryl aldehyde substrates and aryl iodide coupling partners were suitable for this reaction, giving the corresponding masked biaryl aldehydes **81** in satisfactory yields. Compounds **81** can be unmasked to yield biaryl aldehydes **82** in heated TBAF solution.

3.2.4. Acetal-Based Quinolines as Directing Groups

In 2017, Ferreira and co-workers reported on the *meta*-selective C–H arylation of benzyl alcohol derived acetal substrates **83** (Scheme 21).[32] The unique acetal-based quinoline-type directing group (QuA), the distinct amino acid

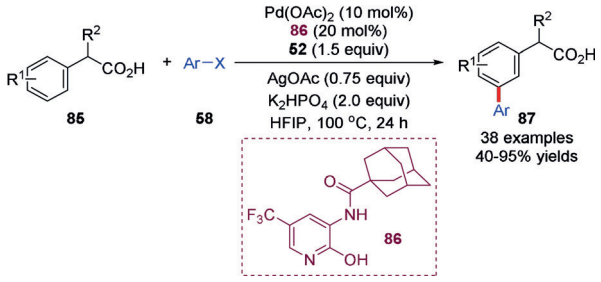


Scheme 21. *meta*-Selective C–H arylation of benzyl alcohol derivatives.

derived ligand *N*-trifluoroacetylglycine (TFA-Gly-OH) as well as Yu mediator **52** were found to be pivotal for the reaction. This transformation exhibited excellent functional group compatibility, and the corresponding biaryl compounds were afforded in moderate to high yields. In addition, the *meta* arylation can be combined with *ortho* arylation or olefination to yield polysubstituted arenes, providing a versatile platform for the diversification of aromatic systems. Moreover, the directing group QuA can be readily cleaved and recovered under very mild reaction conditions.

3.2.5. Free Carboxylic Acids as Directing Groups

In 2017, the more challenging auxiliary-free *meta* C–H arylation of free arylacetic acids **85** was realized by the Yu group (Scheme 22).[33] In this reaction, the choice of a suitable

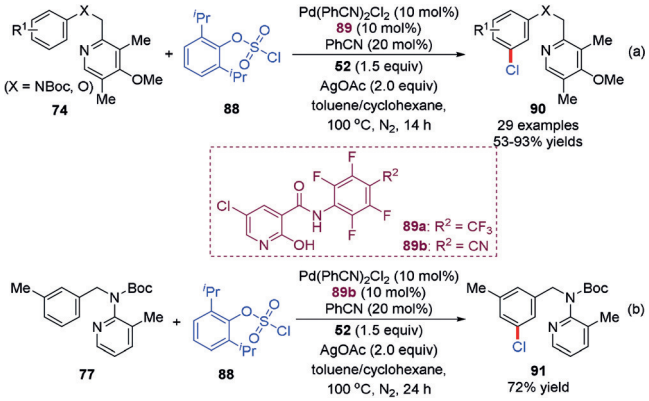


Scheme 22. *meta*-Selective C–H arylation of free phenylacetic acids.

monoprotected 3-amino-2-hydroxypyridine-type ligand **86** and the Yu mediator **52** had a significant influence on the reaction efficiency. Notably, a wide range of aryl iodides, including those with non-coordinating substituents (20 examples), displayed good reactivity to give the corresponding products **87** in moderate to high yields.

3.3. meta*-Selective C–H Chlorination*

The direct C–H chlorination of arenes is an appealing process to access synthetically versatile aryl chlorides. In 2016, the Yu group developed a *meta*-selective C–H chlorination of aniline and phenol derivatives with a pyridine-type tether as the directing group that is co-catalyzed by Pd^{II} and Yu mediator **52** (Scheme 23 a).[34] Aryl chlorosulfate **88** was exploited as the chlorination reagent, and the unique pyridine



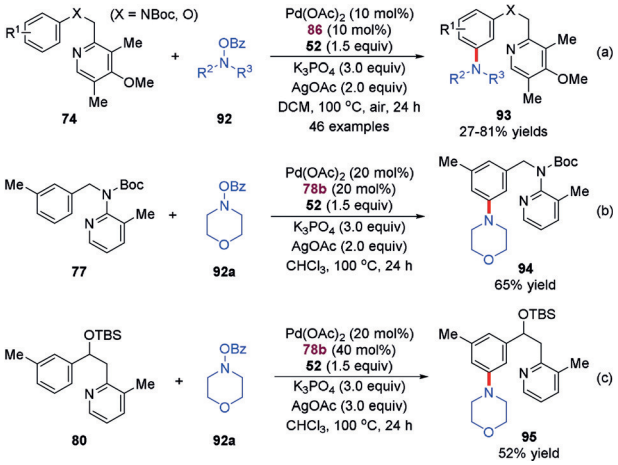
Scheme 23. *meta*-Selective C–H chlorination of aniline, phenol, and benzylamine derivatives.

derivative **89** acted as the ligand of choice. Under the optimized reaction conditions, a large number of substrates bearing various functional groups were tolerated, delivering the corresponding *meta*-chlorinated products **90** in good to excellent yields. Notably, some medicinally important heterocyclic compounds, such as indole, thiophene, and indazole derivatives, are also competent substrates. Moreover, the chlorinated products were transformed into a wide range of synthetically useful synthons that are difficult to access through direct *meta* C–H functionalization, for example, borylation and alkoxylation. Using a similar strategy, the *meta*-selective C–H chlorination of benzylamine derivative **77**

with an N-substituted pyridine-type directing group was also achieved by the same group in 2017 (Scheme 23b).[30]

3.4. meta-*Selective C–H Amination*

Aromatic amines are important structural motifs that are widely found in bioactive natural products, pharmaceuticals, agrochemicals, and materials.[35] The transition-metal-catalyzed C–H amination of arenes has emerged as a powerful and efficient strategy to access aromatic amines.[36] In 2016, the Yu group reported the first example of a Pd^{II}/NBE cooperatively catalyzed *meta* C–H amination of aniline and phenol derivatives tethering a specially designed pyridine-type directing group (Scheme 24a).[37] They found that the

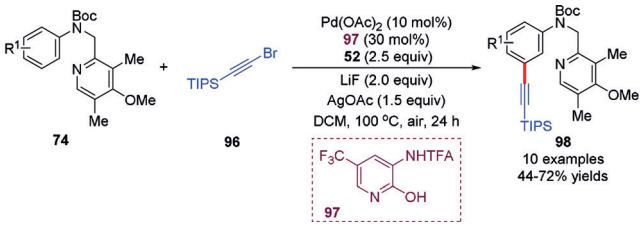


Scheme 24. *meta*-Selective C–H amination of aniline, phenol, benzylamine derivatives and masked aromatic aldehydes.

combination of 3-amino-2-hydroxypyridine-type ligand **86** and Yu mediator **52** was crucial for this transformation, and a large number of *meta*-aminated products (46 examples) were obtained in moderate to good yields. In a similar fashion, the same group also disclosed the successful *meta* C–H amination of benzylamine derivative **77** and masked aryl aldehyde **80**, both with a pyridine-type directing group (Scheme 24b,c).[30,31]

3.5. meta-*Selective C–H Alkynylation*

The only example of a Pd^{II}/NBE co-catalyzed *meta*-selective C–H alkynylation of anilines with a pyridine-derived tether as the directing group was reported by Yu and co-workers in 2016 (Scheme 25).[37] By using pyridine-based ligand **97** and LiF as the additive, the reactivity and selectivity (*meta* versus *ortho* alkynylation) of the reaction was greatly improved. Under the optimized reaction conditions, aniline substrates with diverse functional groups were tolerated, providing the desired *meta*-C–H-alkynylated products in moderate to good yields. It should be noted that except for bulky silyl-protected alkynyl bromides, simple alkyl and

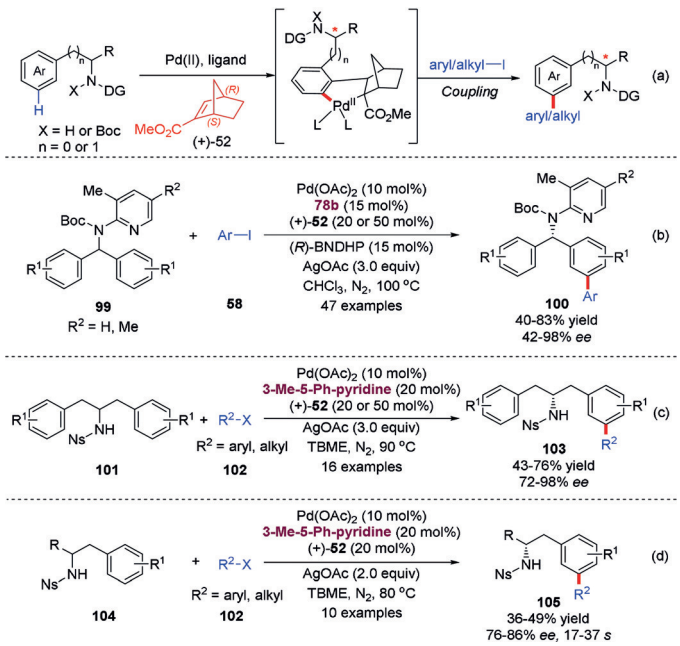


Scheme 25. *meta*-Selective C–H alkynylation of aniline derivatives.

aryl alkynyl bromides as the alkynylating reagents only gave trace amounts of the corresponding products.

3.6. *Enantioselective* meta *C–H Functionalization*

Enantioselective remote C–H functionalization is one of the most challenging yet fascinating directions in organic synthesis. In this context, an impressive breakthrough was recently reported by Yu and co-workers regarding an elegant enantioselective *meta* C–H arylation and alkylation of diarylmethylamines and homobenzylamines by the cooperative catalysis of Pd^{II} and the chiral Yu mediator (+)-**52** (Scheme 26).[38] In these processes, the enantioselective differentiation is based on a fast, reversible, and racemic *ortho* C–H activation followed by stereoselective norbornene insertion and *meta* C–H activation. (+)-**52** served both as a mediator and an efficient chiral source to realize stereoisomeric differentiation of the racemic *ortho* C–H palladation intermediates to control the enantioselectivity (Scheme 26a). This asymmetric *meta* C–H arylation reaction exhibited a broad substrate scope and high enantioselectivities. A broad range of prochiral benzylamines **99** with pyridine-type N substituents as the directing group, prochiral *N*-nosyl homobenzylamines **101,** and racemic *N*-nosyl homobenzyl-

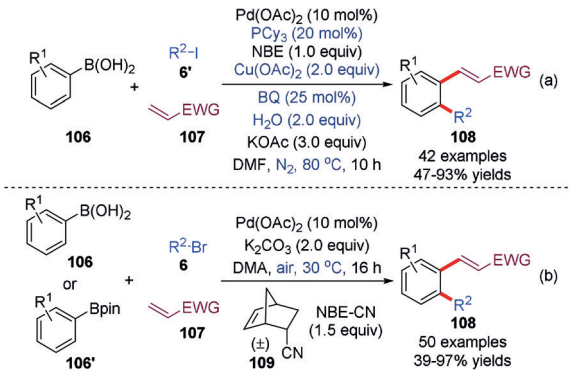


Scheme 26. Enantioselective *meta* C–H arylation and alkylation.

amines **104** as well as diverse aryl iodide coupling reagents were tolerated in this process. In addition to aryl iodides, one aryl bromide, methyl 2-bromobenzoate, was also identified as a competent arylating reagent, giving the desired product in moderate yield and excellent enantioselectivity. In the case of asymmetric *meta* C–H arylation of **99** by desymmetrization, it was found that the enantioselectivity can be dramatically enhanced by the use of (*R*)-BNDHP (1,1′-binaphthyl-2,2′-diyl hydrogen phosphate) as an additive (Scheme 26b). Furthermore, enantioselective *meta* C–H alkylation was also realized for **101** (by desymmetrization) and **104** (by kinetic resolution), by using ethyl iodoacetate or iodomethane as the reagent (Scheme 26c,d). These achievements realized through the cooperative catalysis of Pd^{II} and an enantiopure NBE-type mediator will open a new avenue for enantioselective remote C–H functionalization—one of the most challenging processes in asymmetric catalysis.

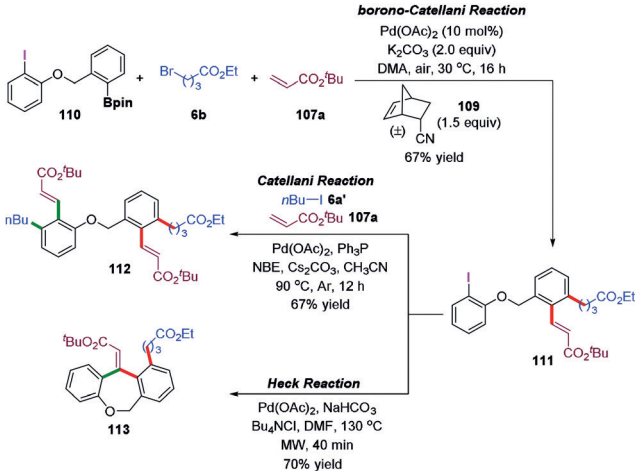
4. Borono-Catellani Reactions

Aryl boronic acids and their derivatives are readily available and very useful organic reagents. In classical Catellani-type reactions, aryl boronic acids and their derivatives mainly act as terminating reagents.[5] Inspired by previously reported Pd^{II}/NBE cooperative catalysis chemistry, the groups of Zhang[39] and Zhou[40] independently reported a novel Pd^{II}-initiated Catellani-type reaction that utilized these widely accessible reagents as the substrates instead of conventional aryl halides to react with alkyl halides (mainly bromides and iodides) and olefins, which was named a "borono-Catellani reaction" (Scheme 27). In Zhang's work, the reaction was performed under N_2 atmosphere at 80 °C, with $Cu(OAc)_2$ as the oxidant to regenerate the Pd^{II} catalyst. Interestingly, it was found that adding 2 equivalents of water and 25 mol % of benzoquinone (BQ) as additives significantly improved the reaction efficiency (Scheme 27a). In contrast, the Zhou group provided more practical reaction conditions: The reaction was run at ambient temperature (30 °C) under air (open flask) while neither phosphine ligand nor additive was needed (Scheme 27b). In addition, the commercially available NBE derivative **109** was introduced as a novel mediator to promote this process for the first time.



Scheme 27. The Pd^{II}-initiated borono-Catellani reaction.

The Zhou group demonstrated the "orthogonal reactivity" of the traditional Pd^0-initiated Catellani reaction and the Pd^{II}-initiated borono-Catellani reaction, by using a rationally designed bifunctional reagent **110** containing both an iodo and a Bpin group as the model substrate. As shown in Scheme 28, **110** reacted with bromide **6b** and *tert*-butyl

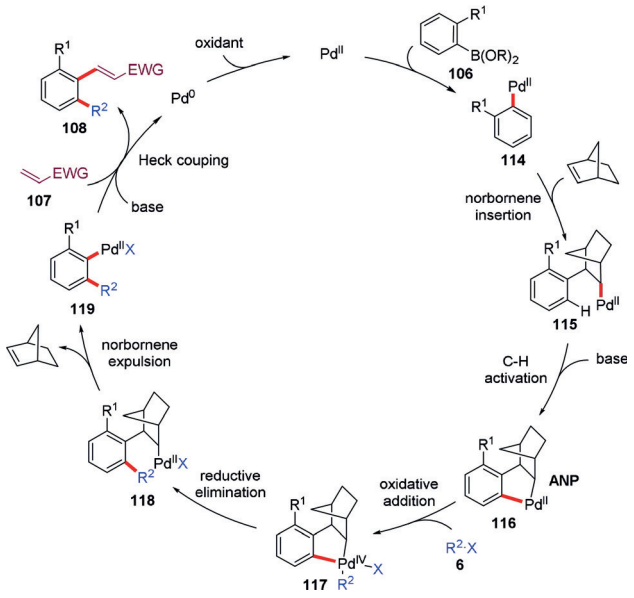


Scheme 28. Orthogonal reactivity of the borono-Catellani and the Catellani reaction.

acrylate **107a** under the standard borono-Catellani reaction conditions to provide the borono-Catellani product **111** in 67 % yield, with no classical Catellani product observed. The intact iodo group in **111** enabled an ensuing classical Catellani reaction to provide the product **112** in 67 % yield. Moreover, **111** underwent a microwave-promoted intramolecular Heck reaction[41] to afford the complex polycyclized product **113** in good yield.

The proposed reaction mechanism of the borono-Catellani reaction is shown in Scheme 29. The catalytic cycle is initiated by the Pd^{II} catalyst, which reacts with aryl boronic acid **106** to provide aryl–Pd^{II} species **114** by transmetalation. The migratory insertion of NBE and subsequent *ortho* C–H activation with the aid of a base gives the key ANP complex **116**. Oxidative addition of alkyl halide **6** to **116** forms Pd^{IV} complex **117**, which then undergoes reductive elimination and subsequent expulsion of NBE to deliver Pd^{II} species **119**. Finally, **119** couples with olefin **107** to provide the Catellani product **108** and release a Pd^0 species, which is then reoxidized to regenerate the Pd^{II} catalyst. Thus an oxidant is needed to promote the catalytic cycle.

It should be pointed out that the requirement for a stoichiometric oxidant actually poses a big challenge to the borono-Catellani reaction as multiple possible side reactions of aryl boronic acids have been reported to proceed under the reaction conditions, including a direct oxidative Heck reaction between the aryl boronic acid and the olefin,[42] oxidative homocoupling,[43] oxidation to phenols,[44] and protolytic deboronation.[44] The success of this borono-Catellani reaction relies on the carefully optimized reaction conditions to minimize the possible side reactions.



Scheme 29. Proposed reaction mechanism for the borono-Catellani reaction.

5. Summary and Outlook

In this Minireview, we have summarized Pd^{II}-initiated Catellani-type reactions (Pd^{II}/NBE cooperative catalysis) and their application in organic synthesis. As described above, substantial efforts have been devoted to this fascinating process, and significant advancements have been made in the past few years. Pd^{II}/NBE cooperative catalysis has been demonstrated to be a powerful complement to the classical Catellani-type reactions. Utilizing this strategy, NH-indoles and NH-pyrroles, (hetero)arenes bearing an *ortho* directing group, as well as aryl boronic acids and derivatives thereof have become suitable substrates that undergo highly selective functionalizations to afford valuable polysubstituted aromatic compounds in a straightforward fashion.

Despite these remarkable advances, the Pd^{II}-initiated Catellani-type reaction is still in its infancy for the following reasons. First, only a few NBE-type mediators have been developed thus far. Currently, only NBE and the Yu mediator **52** are widely used. Meanwhile, stoichiometric quantities of mediators are usually required to achieve good reaction efficiency. Therefore, it is highly desirable to develop more powerful catalytic mediators that allow the Catellani-type processes to occur in a more efficient way. Second, with regard to the development of enantioselective Pd^{II}-initiated Catellani-type reaction, only one example has been reported to date by the Yu group. Nevertheless, this inspiring work serves as an excellent demonstration of the power of chiral mediator/Pd^{II} cooperative catalysis for remote stereocontrol. Third, beyond the three types of substrates developed, there is still much room for exploration to expand the applicability of this process.

Considering the vast synthetic potential of Pd^{II}/NBE cooperative catalysis, future efforts should be invested in the above directions. We anticipate that palladium(II)-initiated Catellani-type reactions will be flourishing in the near future.

Acknowledgements

We are grateful to the National Natural Science Foundation of China (Grants 21602161, 21871213, 21801193), the National "1000-Youth Talents Plan", the Innovation Team Program of Wuhan University (Program No. 2042017kf0232), start-up funding from Wuhan University, and the China Postdoctoral Science Foundation (2016M602339, 2018M642894) for financial support.

Conflict of interest

The authors declare no conflict of interest.

How to cite: *Angew. Chem. Int. Ed.* **2019**, *58*, 5832–5844
Angew. Chem. **2019**, *131*, 5890–5902

[1] a) B. M. Trost, *Science* **1983**, *219*, 245–250; b) P. A. Wender, B. L. Miller, *Nature* **2009**, *460*, 197–201.
[2] a) K. Godula, D. Sames, *Science* **2006**, *312*, 67–72; b) I. V. Seregina, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, *36*, 1173–1193; c) J.-Q. Yu, Z. Shi, *C-H Activation*, Springer, Berlin, **2010**; d) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788–802; e) S. R. Neufeldt, M. S. Sanford, *Acc. Chem. Res.* **2012**, *45*, 936–946; f) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369–375.
[3] M. Catellani, F. Frignani, A. Rangoni, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 119–122; *Angew. Chem.* **1997**, *109*, 142–145.
[4] a) M. Lautens, S. Piguel, *Angew. Chem. Int. Ed.* **2000**, *39*, 1045–1046; *Angew. Chem.* **2000**, *112*, 1087–1088; b) S. Pache, M. Lautens, *Org. Lett.* **2003**, *5*, 4827–4830.
[5] For related reviews, see: a) M. Catellani, E. Motti, N. Della Ca′, *Acc. Chem. Res.* **2008**, *41*, 1512–1522; b) A. Martins, B. Mariampillai, M. Lautens, *Top. Curr. Chem.* **2010**, *292*, 1–33; c) R. Ferraccioli, *Synthesis* **2013**, *45*, 581–591; d) J. Ye, M. Lautens, *Nat. Chem.* **2015**, *7*, 863–870; e) H. Zhu, C. Ye, Z. Chen, *Chin. J. Org. Chem.* **2015**, *35*, 2291–2300; f) N. Della Ca', M. Fontana, E. Motti, M. Catellani, *Acc. Chem. Res.* **2016**, *49*, 1389–1400; g) D.-S. Kim, W.-J. Park, C.-H. Jun, *Chem. Rev.* **2017**, *117*, 8977–9015; h) Z. Nairoukh, M. Cormier, I. Marek, *Nat. Rev. Chem.* **2017**, *1*, 0035; i) P. Gandeepan, L. Ackermann, *Chem* **2018**, *4*, 199–222; j) M. Wegmann, M. Henkel, T. Bach, *Org. Biomol. Chem.* **2018**, *16*, 5376–5385; for selected recent works, see: k) Z.-S. Liu, Q. Gao, H.-G. Cheng, Q. Zhou, *Chem. Eur. J.* **2018**, *24*, 15461–15476; l) F. Liu, Z. Dong, J. Wang, G. Dong, *Angew. Chem. Int. Ed.* **2019**, *58*, 2144–2148; *Angew. Chem.* **2019**, *131*, 2166–2170; m) R. Li, G. Dong, *Angew. Chem. Int. Ed.* **2018**, *57*, 1697–1701; *Angew. Chem.* **2018**, *130*, 1713–1717; n) H.-G. Cheng, C. Wu, H. Chen, R. Chen, G. Qian, Z. Geng, Q. Wei, Y. Xia, J. Zhang, Y. Zhang, Q. Zhou, *Angew. Chem. Int. Ed.* **2018**, *57*, 3444–3448; *Angew. Chem.* **2018**, *130*, 3502–3506; o) Z.-S. Liu, G. Qian, Q. Gao, P. Wang, H.-G. Cheng, Q. Wei, Q. Liu, Q. Zhou, *ACS Catal.* **2018**, *8*, 4783–4788; p) L. Bai, J. Liu, W. Hu, K. Li, Y. Wang, X. Luan, *Angew. Chem. Int. Ed.* **2018**, *57*, 5151–5155; *Angew. Chem.* **2018**, *130*, 5245–5249; q) G. Qian, M. Bai, S. Gao, H. Chen, S. Zhou, H.-G. Cheng, W. Yan, Q. Zhou, *Angew. Chem. Int. Ed.* **2018**, *57*, 10980–10984; *Angew. Chem.* **2018**, *130*, 11146–11150.
[6] a) G. Maestri, E. Motti, N. Della Ca', M. Malacria, E. Derat, M. Catellani, *J. Am. Chem. Soc.* **2011**, *133*, 8574–8585; b) D. I. Chai, P. Thansandote, M. Lautens, *Chem. Eur. J.* **2011**, *17*, 8175–8188.
[7] L. Jiao, T. Bach, *J. Am. Chem. Soc.* **2011**, *133*, 12990–12993.
[8] a) L. Jiao, E. Herdtweck, T. Bach, *J. Am. Chem. Soc.* **2012**, *134*, 14563–14572; b) L. Jiao, T. Bach, *Synthesis* **2014**, *46*, 35–41.

[9] H. K. Potukuchi, T. Bach, *J. Org. Chem.* **2013**, *78*, 12263 – 12267.
[10] H. Zhang, H.-Y. Wang, Y. Luo, C. Chen, Y. Cao, P. Chen, Y.-L. Guo, Y. Lan, G. Liu, *ACS Catal.* **2018**, *8*, 2173 – 2180.
[11] M. Mizutani, S. Yasuda, C. Mukai, *Chem. Commun.* **2014**, *50*, 5782 – 5785.
[12] S.-Z. Jiang, X.-Y. Zeng, X. Liang, T. Lei, K. Wei, Y.-R. Yang, *Angew. Chem. Int. Ed.* **2016**, *55*, 4044 – 4048; *Angew. Chem.* **2016**, *128*, 4112 – 4116.
[13] T. Xiao, Z.-T. Chen, L.-F. Deng, D. Zhang, X.-Y. Liu, H. Song, Y. Qin, *Chem. Commun.* **2017**, *53*, 12665 – 12667.
[14] Y. Gao, W. Zhu, L. Yin, B. Dong, J. Fu, Z. Ye, F. Xue, C. Jiang, *Tetrahedron Lett.* **2017**, *58*, 2213 – 2216.
[15] L. Jiao, T. Bach, *Angew. Chem. Int. Ed.* **2013**, *52*, 6080 – 6083; *Angew. Chem.* **2013**, *125*, 6196 – 6199.
[16] For selected reviews, highlights, and book chapters, see: a) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 5094 – 5115; *Angew. Chem.* **2009**, *121*, 5196 – 5217; b) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147 – 1169; c) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624 – 655; d) J. Wencel-Delord, T. Dröge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740 – 4761; e) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651 – 3678; f) J. Li, S. D. Sarkar, L. Ackermann, *Top. Organomet. Chem.* **2015**, *55*, 217 – 257; g) Y. Yuan, S. Song, N. Jiao, *Acta Chim. Sinica* **2015**, *73*, 1231; h) L. Ping, D. S. Chung, J. Bouffard, S. Lee, *Chem. Soc. Rev.* **2017**, *46*, 4299 – 4328; i) *Strategies for Palladium-Catalyzed Non-Directed and Directed C–H Bond Functionalization* (Ed.: A. R. Kapdi, D. Maiti), Elsevier, Amsterdam, **2017**.
[17] For selected examples, see: a) Y. Kuninobu, H. Ida, M. Nishi, M. Kanai, *Nat. Chem.* **2015**, *7*, 712 – 717; b) R. Bisht, B. Chattopadhyay, *J. Am. Chem. Soc.* **2016**, *138*, 84 – 87; c) H. J. Davis, M. T. Mihai, R. J. Phipps, *J. Am. Chem. Soc.* **2016**, *138*, 12759 – 12762; d) H. J. Davis, G. R. Genov, R. J. Phipps, *Angew. Chem. Int. Ed.* **2017**, *56*, 13351 – 13355; *Angew. Chem.* **2017**, *129*, 13536 – 13540; e) M. T. Mihai, H. J. Davis, G. R. Genov, R. J. Phipps, *ACS Catal.* **2018**, *8*, 3764 – 3769; f) R. Bisht, M. E. Hoque, B. Chattopadhyay, *Angew. Chem. Int. Ed.* **2018**, *57*, 15762 – 15766; *Angew. Chem.* **2018**, *130*, 15988 – 15992.
[18] For a related review, see: a) J. A. Leitch, C. G. Frost, *Chem. Soc. Rev.* **2017**, *46*, 7145 – 7153; for selected examples, see: b) O. Saidi, J. Marafie, A. E. W. Ledger, P. M. Liu, M. F. Mahon, G. Kociok-Köhn, M. K. Whittlesey, C. G. Frost, *J. Am. Chem. Soc.* **2011**, *133*, 19298 – 19301; c) N. Hofmann, L. Ackermann, *J. Am. Chem. Soc.* **2013**, *135*, 5877 – 5884; d) C. J. Teskey, A. Y. W. Lui, M. F. Greaney, *Angew. Chem. Int. Ed.* **2015**, *54*, 11677 – 11680; *Angew. Chem.* **2015**, *127*, 11843 – 11846; e) J. Li, S. Warratz, D. Zell, S. D. Sarkar, E. E. Ishikawa, L. Ackermann, *J. Am. Chem. Soc.* **2015**, *137*, 13894 – 13901; f) Z. Fan, J. Ni, A. Zhang, *J. Am. Chem. Soc.* **2016**, *138*, 8470 – 8475; g) J. Li, K. Korvorapun, S. D. Sarkar, T. Rogge, D. J. Burns, S. Warratz, L. Ackermann, *Nat. Commun.* **2017**, *8*, 15430 – 15437; h) K. Korvorapun, N. Kaplaneris, T. Rogge, S. Warratz, A. C. Stückl, L. Ackermann, *ACS Catal.* **2018**, *8*, 886 – 892.
[19] For selected examples, see: a) D. Leow, G. Li, T.-S. Mei, J.-Q. Yu, *Nature* **2012**, *486*, 518 – 522; b) R. Tang, G. Li, J.-Q. Yu, *Nature* **2014**, *507*, 215 – 220; c) L. Wan, N. Dastbaravardeh, G. Li, J.-Q. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 18056 – 18059; d) L. Chu, M. Shang, K. Tanaka, Q. Chen, N. Pissarnitski, E. Streckfuss, J.-Q. Yu, *ACS Cent. Sci.* **2015**, *1*, 394 – 399; e) M. Bera, A. Maji, S. K. Sahoo, D. Maiti, *Angew. Chem. Int. Ed.* **2015**, *54*, 8515 – 8519; *Angew. Chem.* **2015**, *127*, 8635 – 8639; f) A. Maji, B. Bhaskararao, S. Singha, R. B. Sunoj, D. Maiti, *Chem. Sci.* **2016**, *7*, 3147 – 3153; g) Z. Zhang, K. Tanaka, J.-Q. Yu, *Nature* **2017**, *543*, 538 – 542.
[20] X.-C. Wang, W. Gong, L.-Z. Fang, R.-Y. Zhu, S. Li, K. M. Engle, J.-Q. Yu, *Nature* **2015**, *519*, 334 – 338.
[21] P.-X. Shen, X.-C. Wang, P. Wang, R.-Y. Zhu, J.-Q. Yu, *J. Am. Chem. Soc.* **2015**, *137*, 11574 – 11577.
[22] G. Cheng, P. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2017**, *56*, 8183 – 8186; *Angew. Chem.* **2017**, *129*, 8295 – 8298.
[23] J. Liu, Q. Ding, W. Fang, W. Wu, Y. Zhang, Y. Peng, *J. Org. Chem.* **2018**, *83*, 13211 – 13216.
[24] a) P. J. Hajduk, M. Bures, J. Praestgaard, S. W. Fesik, *J. Med. Chem.* **2000**, *43*, 3443 – 3447; b) D. A. Horton, G. T. Bourne, M. L. Smythe, *Chem. Rev.* **2003**, *103*, 893 – 930; c) J. Klekota, F. P. Roth, *Bioinformatics* **2008**, *24*, 2518 – 2525.
[25] a) J. Han, L. Zhang, Y. Zhu, Y. Zheng, X. Chen, Z.-B. Huang, D.-Q. Shi, Y. Zhao, *Chem. Commun.* **2016**, *52*, 6903 – 6906; b) J. Han, N. Wang, Z.-B. Huang, Y. Zhao, D.-Q. Shi, *Org. Biomol. Chem.* **2017**, *15*, 5112 – 5116.
[26] P.-X. Ling, K. Chen, B.-F. Shi, *Chem. Commun.* **2017**, *53*, 2166 – 2169.
[27] Q. Ding, S. Ye, G. Cheng, P. Wang, M. E. Farmer, J.-Q. Yu, *J. Am. Chem. Soc.* **2017**, *139*, 417 – 425.
[28] Z. Dong, J. Wang, G. Dong, *J. Am. Chem. Soc.* **2015**, *137*, 5887 – 5890.
[29] P. Wang, M. E. Farmer, X. Huo, P. Jain, P.-X. Shen, M. Ishoey, J. E. Bradner, S. R. Wisniewski, M. E. Eastgate, J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, *138*, 9269 – 9276.
[30] P. Wang, M. E. Farmer, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2017**, *56*, 5125 – 5129; *Angew. Chem.* **2017**, *129*, 5207 – 5211.
[31] M. E. Farmer, P. Wang, H. Shi, J.-Q. Yu, *ACS Catal.* **2018**, *8*, 7362 – 7367.
[32] Q. Li, E. M. Ferreira, *Chem. Eur. J.* **2017**, *23*, 11519 – 11523.
[33] G.-C. Li, P. Wang, M. E. Farmer, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2017**, *56*, 6874 – 6877; *Angew. Chem.* **2017**, *129*, 6978 – 6981.
[34] H. Shi, P. Wang, S. Suzuki, M. E. Farmer, J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, *138*, 14876 – 14879.
[35] a) J. Cheng, K. Kamiya, I. Kodama, *Cardiovasc. Drug Rev.* **2001**, *19*, 152 – 171; b) C. Sánchez, C. Méndez, J. A. Salas, *Nat. Prod. Rep.* **2006**, *23*, 1007 – 1045.
[36] a) F. Paul, J. Patt, J. F. Hartwig, *J. Am. Chem. Soc.* **1994**, *116*, 5969 – 5970; b) A. S. Guram, S. L. Buchwald, *J. Am. Chem. Soc.* **1994**, *116*, 7901 – 7902; c) J. P. Wolfe, S. Wagaw, J. F. Marcoux, S. L. Buchwald, *Acc. Chem. Res.* **1998**, *31*, 805 – 818; d) J. F. Hartwig, *Acc. Chem. Res.* **1998**, *31*, 852 – 860; e) Z. Dong, G. Dong, *J. Am. Chem. Soc.* **2013**, *135*, 18350 – 18353.
[37] P. Wang, G.-C. Li, P. Jain, M. E. Farmer, J. He, P.-X. Shen, J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, *138*, 14092 – 14099.
[38] H. Shi, A. N. Herron, Y. Shao, Q. Shao, J.-Q. Yu, *Nature* **2018**, *558*, 581 – 585.
[39] G. Shi, C. Shao, X. Ma, Y. Gu, Y. Zhang, *ACS Catal.* **2018**, *8*, 3775 – 3779.
[40] S. Chen, Z.-S. Liu, T. Yang, Y. Hua, Z. Zhou, H.-G. Cheng, Q. Zhou, *Angew. Chem. Int. Ed.* **2018**, *57*, 7161 – 7165; *Angew. Chem.* **2018**, *130*, 7279 – 7283.
[41] a) M. Larhed, C. Moberg, A. Hallberg, *Acc. Chem. Res.* **2002**, *35*, 717 – 727; b) C. O. Kappe, *Angew. Chem. Int. Ed.* **2004**, *43*, 6250 – 6284; *Angew. Chem.* **2004**, *116*, 6408 – 6443.
[42] a) T. Kurahashi, H. Shinokubo, A. Osuka, *Angew. Chem. Int. Ed.* **2006**, *45*, 6336 – 6338; *Angew. Chem.* **2006**, *118*, 6484 – 6486; b) K. S. Yoo, C. H. Yoon, K. W. Jung, *J. Am. Chem. Soc.* **2006**, *128*, 16384 – 16393; c) J. D. Crowley, K. D. Hänni, A.-L. Lee, D. A. Leigh, *J. Am. Chem. Soc.* **2007**, *129*, 12092 – 12903; d) S. Sakaguchi, K. S. Yoo, J. O'Neill, J. H. Lee, T. Stewart, K. W. Jung, *Angew. Chem. Int. Ed.* **2008**, *47*, 9326 – 9329; *Angew. Chem.* **2008**, *120*, 9466 – 9469.
[43] M. Kotora, T. Takahashi in *Handbook of Organopalladium Chemistry for Organic Synthesis*, *Vol. 1* (Ed.: E.-i. Negishi), Wiley, New York, **2002**, pp. 973 – 993.
[44] D. V. Partyka, *Chem. Rev.* **2011**, *111*, 1529 – 1541.

Manuscript received: November 27, 2018
Accepted manuscript online: December 27, 2018
Version of record online: February 20, 2019

