EDGE ARTICLE

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Redox-neutral *ortho*-C–H amination of pinacol arylborates *via* palladium(II)/norbornene catalysis for aniline synthesis†

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A palladium(II)/norbornene cooperative catalysis enabled redox-neutral *ortho*-C–H amination of pinacol aryl- or heteroarylborates for the synthesis of structurally diverse anilines is reported. This method is scalable, robust (tolerance of air and moisture), phosphine ligand-free, and compatible with a wide range of functionalities. These practical features make this reaction amenable for industry. A plethora of synthetically very useful halogenated anilines, which often cannot be prepared *via* other transition-metal-catalyzed aminations, are readily produced using this method. Particularly, the orthogonal reactivity between pinacol arylborates and aryl iodides is demonstrated. Preliminary deuterium-labeling studies reveal a redox-neutral *ipso*-protonation mechanism of this process, which will surely inspire the future development of this field. Overall, the exceptionally broad scope (47 examples) and reliability of this procedure, together with the wide availability of pinacol arylborates, make this chemistry a valuable addition to the existing methods for aniline synthesis.

Functionalized anilines have attracted considerable attention as a result of their widely applications in the pharmaceutical industry and medicinal chemistry.[1] For example, popular marketed medicines aripiprazole (antipsychotics),[1b] repaglinide (anti-type II diabetes),[1c] linezolid (antibacterial),[1d] and EphB4 kinase inhibitors[1e] all contain an aniline motif as the pharmacophore (Fig. 1). Therefore, general methods for the assembly of these motifs are highly desirable. Synthesis of anilines through C–N bond formation is the most widely adopted strategy, and substantial progress has been made over the past two decades.[2–5] Among these approaches, palladium-catalyzed

aminations play a significant role.[3–5] For example, the famous Buchwald–Hartwig *ipso*-amination[3] that allows the facile synthesis of anilines from aryl halides and nucleophilic amines (Scheme 1A). In 2013, the Dong group reported an elegant palladium(0)/norbornene (NBE) cooperative catalysis (the Catellani reaction)[6] enabled *ortho*-C–H amination of aryl iodides (the Dong amination), utilizing electrophilic *O*-benzoyl hydroxylamines as the amination reagents and isopropanol as the proton source for *ipso*-termination.[4] Later on, they extended this chemistry to *ortho*-C–H amination of aryl bromides (Scheme 1B).[5] The Dong amination represents a nice complement to the Buchwald–Hartwig *ipso*-amination for the preparation of *meta*-substituted anilines, while it requires a stoichiometric reductant for the recovery of the palladium(0) catalyst. Recently, the group of Zhang and our group concurrently reported the *ortho*-C–H alkylation of the arylboronic acids and their derivatives (instead of aryl halides) *via* the palladium(II)-initiated Catellani-type reaction (Borono–Catellani reaction).[7] Therein, a stoichiometric oxidant (Cu(OAc)$_2$, air or oxygen) is required for regenerating the palladium(II) catalyst. Based on the chemistry, we envisaged a redox-neutral "Borono–Catellani amination" process for the facile preparation of anilines, with widely accessible arylboronic acids or their derivatives and *O*-benzoyl hydroxylamines as the reactants (Scheme 1C). Prior to the start of this project, redox-neutral Borono–Catellani reactions had not been reported. Until recently, the group of Dong reported elegant related research (Scheme 1D).[8] As shown in Scheme 1C, it is surmised that the
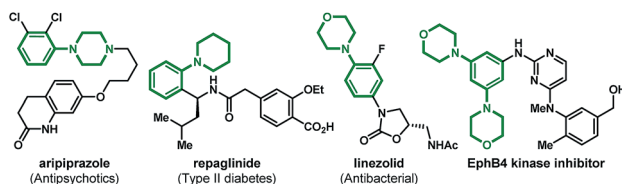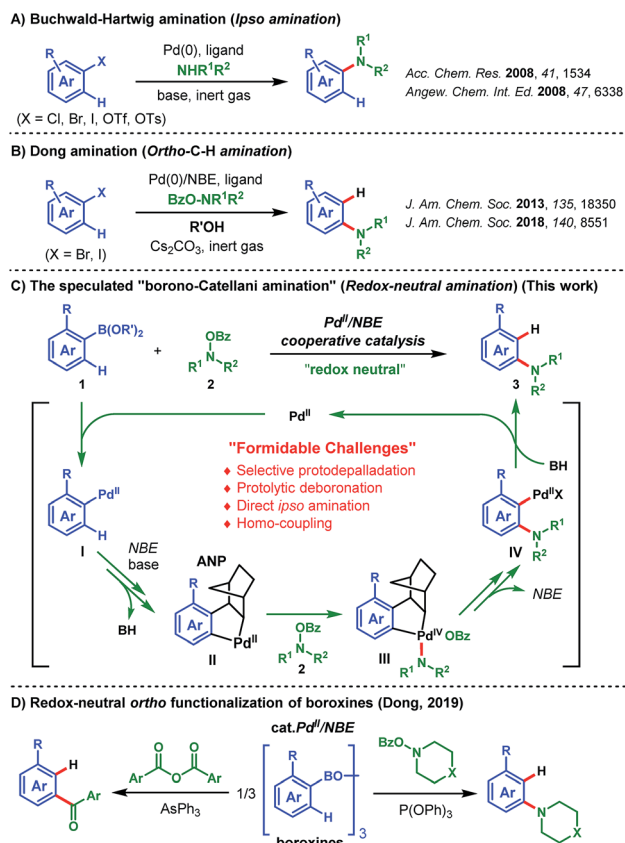

Fig. 1 Biologically important aniline scaffolds.

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A) Buchwald-Hartwig amination (*Ipso* amination)

B) Dong amination (*Ortho*-C-H amination)

C) The speculated "borono-Catellani amination" (*Redox-neutral amination*) (This work)

D) Redox-neutral *ortho* functionalization of boroxines (Dong, 2019)

Scheme 1 Palladium-catalyzed amination strategies for aniline synthesis.

reaction is initiated through transmetalation between the palladium(II) catalyst and arylboronic acid derivative **1** to deliver the aryl palladium(II) intermediate **I**. The following steps involve insertion of NBE to **I** and subsequent *ortho*-C–H activation, generating the aryl/NBE palladacycle complex (ANP) **II**. The oxidative addition of amination reagent **2** to **II** gives the palladium(IV) complex **III**,[9] which then undergoes reductive elimination and successive release of NBE to afford palladium(II) species **IV**. The final reaction termination by protonation[10] of **IV** provides the desired aniline **3** and regenerate the palladium(II) catalyst. The intrinsic advantage of this "Borono–Catellani amination" lies in its "redox-neutral" property: this process involves a Pd(II)–Pd(IV)–Pd(II) catalytic cycle,[11] thus no external oxidant and reductant are needed. This feature constitutes a nice extension of previous Catellani-type reactions.[12] In addition, the widely accessible arylboronic species *versus* aryl halides will guarantee promising synthetic potential of this process for diversified aniline preparation. Although the above process is intriguing and mechanistically feasible, multiple challenges are foreseeable. First, protodepalladation can occur to arylpalladium species (**I**, **II** and **IV**) of the catalytic cycle, which may result in a selectivity issue. Second, transmetalation of arylborates and the following *ortho*-C–H activation are generally promoted by a base, while the final protodepalladation step requires an acid. Hence, the compatibility of these paradoxical steps could be another issue. Third, other

competing side reactions related to arylboronic species (*e.g.* direct *ipso*-amination,[13] protolytic deboronation,[14] and homo-coupling[15]) will also constitute formidable challenges.

To address the aforementioned challenges and realize this intriguing process, a model reaction was set up for the optimization of reaction conditions, with readily available 1-naphthylboronic acid pinacol ester (**1a**) and morpholino benzoate (**2a**) as the reactants. Selected results are summarized in Table 1. Initially, Pd(OAc)$_2$ was chosen as the catalyst (10 mol%), 2-norbornene (NBE) as the mediator, K$_2$CO$_3$ as the base (2.5 equiv.), and DMF as the solvent. Gratifyingly, when the reaction was run at 70 °C in air for 16 h, the desired product **3a** was obtained in 15% yield (entry 1). The following studies focused on screening of the reaction solvent, which was demonstrated to play a critical role in this process (entries 1–4). Only a trace amount of **3a** was detected when nonpolar solvent toluene was used. In contrast, while switching to the polar solvent DMSO, a dramatic increase of yield of **3a** was realized (56%, entry 3). In addition, the screening of other polar solvents did not provide further improvement in the reaction efficiency (see ESI for the details†). The use of DMSO as the solvent was beneficial for the desired reaction on the one hand, but on the other hand, a severe protodeboronation[14] side reaction to yield naphthalene as well as quick decomposition of the amination reagent **2a** also occurred. This was why an overall moderate yield (56%) was obtained. To our delight, after intensive optimizations, this problem was nicely solved by simply employing 1,4-dioxane as the cosolvent (DMSO/dioxane = 2 : 5), and the yield of **3a** was improved to 82% (entry 4). Additional optimizations regarding the base and palladium catalyst did not provide any significant improvement (entries 5–8). Thus, entry 4 was identified as the optimal conditions for this transformation. It is worth mentioning that these optimization studies were all performed in air,[7b] and a following control experiment revealed that air was

Table 1 Optimization of reaction conditions[a]

Entry	[Pd]	Base	Solvent	Yield (%)[b]
1	Pd(OAc)$_2$	K$_2$CO$_3$	DMF	15
2	Pd(OAc)$_2$	K$_2$CO$_3$	Toluene	1
3	Pd(OAc)$_2$	K$_2$CO$_3$	DMSO	56
4	Pd(OAc)$_2$	K$_2$CO$_3$	DMSO/dioxane[c]	82 (84)[d]
5	Pd(OAc)$_2$	KHCO$_3$	DMSO/dioxane[c]	46
6	Pd(OAc)$_2$	KOH	DMSO/dioxane[c]	70
7	PdCl$_2$	K$_2$CO$_3$	DMSO/dioxane[c]	51
8	Pd(TFA)$_2$	K$_2$CO$_3$	DMSO/dioxane[c]	74
9[e]	Pd(OAc)$_2$	K$_2$CO$_3$	DMSO/dioxane[c]	75

[a] The reaction was performed on a 0.1 mmol scale. [b] GC yield with biphenyl as an internal standard. [c] DMSO/dioxane = 2 : 5. [d] Isolated yield in parentheses on a 0.2 mmol scale. [e] The reaction was performed under argon. TFA = trifluoroacetoxy, DMF = N,N-dimethylformamide, and DMSO = dimethylsulfoxide.

beneficial since a tangible drop of yield was observed when running the reaction in argon (entry 9). This interesting phenomenon indicates that on the one hand the desired transformation is indeed a redox-neutral process (no external oxidant is needed). On the other hand, it shows that the presence of air could prohibit the possible palladium(0)-involved side reactions,[15] thus favoring the expected reaction. Additionally, allowing us to perform the reaction in air is very attractive from both the practical and economic perspective. Moreover, this process does not require any phosphine or arsine ligand[7b,c] which is pivotal for previous palladium-catalyzed aminations.[3–5,7a,8] Overall, these practical features make this reaction amenable for industry.
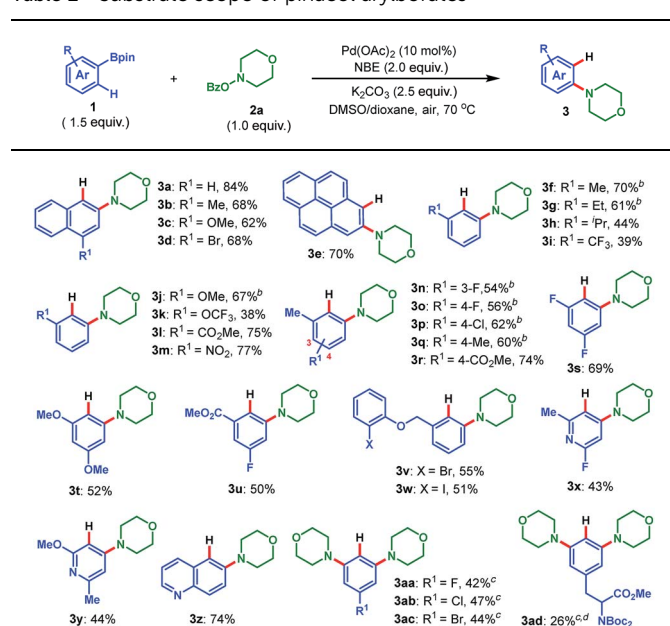
With the optimized conditions in hand, we first examined the scope of pinacol arylborates, employing **2a** as the reaction partner. The results are summarized in Table 2. For *ortho*-substituted pinacol arylborates, both electron-donating (**1f–h**, **1j–k**, **1q**, and **1t**) and electron-withdrawing substitutions (**1i**, **1l–p**, **1r**, and **1u**) on the aromatic rings were compatible, providing *meta*-substituted anilines in moderate to good yields (38–77%). Polycyclic pinacol arylborates (**1a–e**) were also suitable substrates to deliver the corresponding anilines in good yields (62–84%). Notably, pinacol heteroarylborates (**1x–1z**) reacted well with **2a** to afford the desired heteroanilines (**3x–3z**) in 43%, 44% and 74% yield, respectively. For pinacol arylborates without *ortho* substituents, the diaminated products (**3aa–3ad**) were obtained in moderate yields. In particular, the tyrosine-derived pinacol arylborate (**1ad**) could be applied to this reaction, delivering the corresponding unnatural amino acid-type product (**3ad**) in 26% yield. Furthermore, this transformation

possesses excellent chemoselectivity, and a variety of functional groups were tolerated, including fluoro (**3n–3o**, **3s**, **3u**, **3x**, and **3aa**), chloro (**3p** and **3ab**), bromo (**3d**, **3v**, and **3ac**), even iodo (**3w**), methoxyl (**3c**, **3j**, **3t**, and **3y**), trifluoromethyl (**3i**), trifluoromethoxyl (**3k**), ester (**3l**, **3r**, **3u**, and **3ad**), bis-Boc-protected amino (**3ad**), and nitro (**3m**). The compatibility of various functional groups is intriguing, since it would allow further manipulation of the obtained anilines. It is especially noteworthy that a variety of halogenated anilines (**3d**, **3p**, **3v**, **3w**, and **3ab–3ac**), which often cannot be prepared *via* other transition-metal-catalyzed aminations,[3–5] enable further metal-catalyzed cross coupling reactions.[16]

To illustrate the synthetic utility of this protocol, the scope of the amination reagent **2** was then investigated, with pinacol arylborate **1a** as the reaction partner (Table 3). O-Benzoyl hydroxylamines derived from common cyclic amines, such as morpholine (**2a**), piperidine (**2b–2k**), piperazine (**2l–2n**), thiomorpholine (**2o**), pyrrolidine (**2p**) and azepane (**2q**) can all be used in the reaction to afford the corresponding products in moderate to good yields (29–84%). A gamut of functional groups in these amination reagents were tolerated during the process, such as primary alcohol (**2g**), secondary alcohol (**2e**), tertiary alcohol (**2h**), TBS ether (**2f**), ketal (**2i**), ester (**2j** and **2k**), benzoylamino (**2l**) and carbamate (**2m** and **2n**) groups. In addition, the uncyclized amination reagent *N*-benzyl *N*-benzoyl hydroxymethylamine (**2r**) also reacted uneventfully albeit with a moderate yield, which may serve as an alternative way to access the secondary aryl amines through a following debenzylation. It is worth mentioning that the incorporated heterocyclic motifs, *e.g.* morpholine, piperidine, piperazine, pyrrolidine and azepane, are ubiquitous and essentially important in small molecule drug discovery.[17]
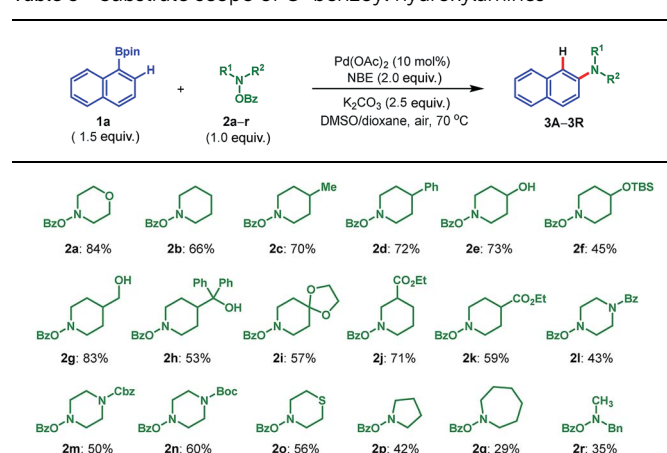
The practicality and robustness of this amination process are demonstrated by the 6.0 mmol scale experiment between **1a** and **2a**, as depicted in Scheme 2A, wherein application of the standard reaction conditions afforded product **3a** in a good yield

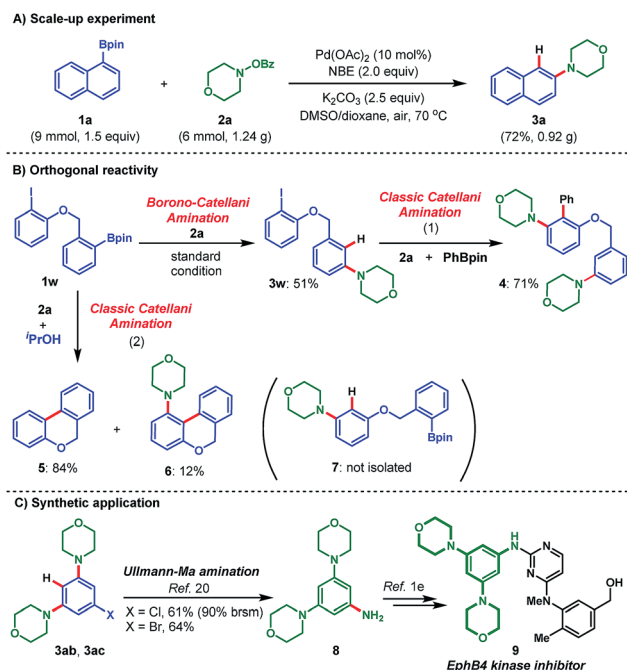**Table 2** Substrate scope of pinacol arylborates[a]

[a] All reactions were performed on a 0.2 mmol scale. Isolated yields were reported. [b] **2a** was added in two portions. [c] 2.0 equiv. of **2a** and 4.0 equiv. of K$_2$CO$_3$ were used. [d] The reaction was performed at 80 °C.

Table 3 Substrate scope of O-benzoyl hydroxylamines[a]

[a] All reactions were performed on a 0.2 mmol scale, and **2** was added in two portions. Isolated yields are reported.
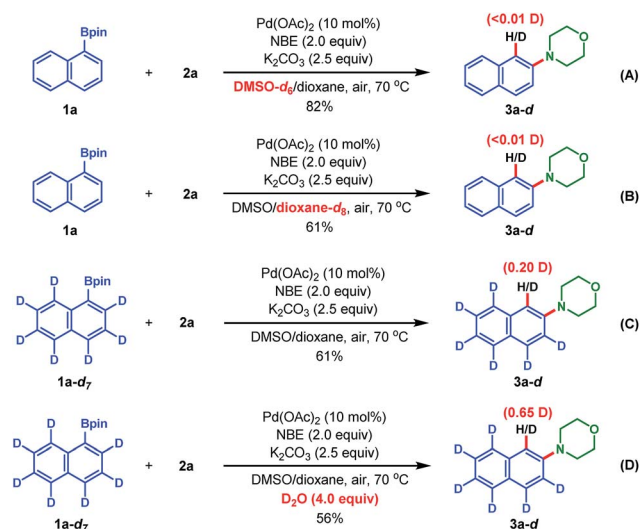
Scheme 2   Scale-up experiment and synthetic applications. Reagents and conditions: (1) Pd(OAc)$_2$, (2-furyl)$_3$P, NBE, Cs$_2$CO$_3$, toluene, 80 °C, Ar, 20 h; (2) Pd(OAc)$_2$, P(pOMe-C$_6$H$_4$)$_3$, NBE, Cs$_2$CO$_3$, toluene, 100 °C, Ar, 24 h.

(72%, 0.92 g). The tolerance of the iodo group in the current Borono–Catellani amination process prompted us to investigate the possible orthogonal reactivity between pinacol arylborate and aryl iodides. The bifunctional reagent **1w** was chosen as the model substrate to verify this hypothesis. Firstly, **1w** reacted with **2a** under the standard Borono–Catellani amination conditions, and the product **3w** was indeed afforded in 51% yield while no classic Catellani-type product was observed. Then, the intact iodo group in **3w** enabled a traditional Catellani reaction[18] to provide the polysubstituted arene **4** in 71% yield. In stark contrast, subjecting **1w** and **2a** to traditional Catellani reaction conditions,[4a] the intramolecular Suzuki–Miyaura coupling product **5** was isolated as the major component, alongside the minor Catellani-type amination product **6** formed through intramolecular Suzuki–Miyaura termination.[18] The Catellani-type *ortho*-C–H amination product **7** generated by protonation termination was not isolated (Scheme 2B). Hence, the orthogonal reactivity between these two types of Catellani reactions was demonstrated.

Furthermore, the synthetic utility of the obtained *ortho*-C–H amination products is shown in Scheme 2C. The 3,5-diaminated aryl halides **3ab** and **3ac** from Table 2 were readily transformed to 3,5-di(morpholino)aniline **8**, the useful common intermediate to prepare various potent EphB4 kinase inhibitors,[19] in good yields through the Ullmann–Ma amination.[20] It is noteworthy that **8** was previously prepared in three steps from expensive starting materials.[21]

Finally, to probe the proton source of the termination step and gain mechanistic insights into this reaction, deuterium-

labeling experiments were performed (Scheme 3). First, an experiment regarding the reaction between **1a** and **2a** in DMSO-d_6 instead of normal DMSO under the standard reaction conditions led to the isolation of product **3a** without any deuterium incorporation (eqn (A)); the same deuterium results were obtained when the 1,4-dioxane-d_8 instead of 1,4-dioxane was used as the cosolvent (eqn (B)). These results indicated that the termination step didn't involve reductive elimination of [ArPdH] species with hydride from the solvents.[22] Then, the fully deuterated **1a**-d_7 (ref. 23) was used as the substrate (see ESI for its preparation†), and 20% deuterium incorporation at the *ipso* position of product **3a** was found (eqn (C)). Lastly, when **1a**-d_7 reacted with **2a** under the standard reaction conditions with 4.0 equiv. of D$_2$O as the additive, **3a** was isolated in a lower yield (56%) but with a significantly increased deuterium incorporation (65%) at the *ipso* position (eqn (D)). These experimental results indicated that both the protons from the *ortho*-C–H of pinacol arylborate and the adventitious water in the reaction system are the sources for the Catellani termination step, but not the solvent DMSO. The reduction of the deuterium incorporation ratio in eqn (C) and (D) was probably due to the facile H–D exchange with water in the reaction system.[8] Thus, these results support the redox-neutral *ipso*-protonation mechanism proposed in Scheme 1C.

Scheme 3   Preliminary mechanistic studies.

Conclusions

In summary, we have developed a palladium(II)/norbornene cooperative catalysis enabled redox-neutral *ortho*-C–H amination of pinacol aryl- or heteroarylborates for the synthesis of structurally diverse anilines. This method is scalable, robust (tolerance of air and moisture), phosphine ligand-free, and compatible with a wide range of functionalities. These practical features make this reaction amenable for industry. It is especially noteworthy that a plethora of synthetically very useful halogenated anilines, which often cannot be prepared *via* other

transition-metal-catalyzed aminations, are readily produced using this method. Particularly, the tolerance of the iodo function enables the orthogonal reactivity between pinacol arylborate and aryl iodides. Preliminary deuterium-labeling studies reveal a redox-neutral *ipso*-protonation mechanism of this process, which will surely inspire the future development of this research field. Overall, the exceptionally broad scope and reliability of this procedure, together with the wide availability of pinacol arylborates, make this chemistry a valuable addition to the existing methods for aniline synthesis.

Conflicts of interest

The authors declare no competing financial interests.

Acknowledgements

Notes and references

1 (a) E. Vitaku, D. T. Smith and J. T. Njardarson, *J. Med. Chem.*, 2014, **57**, 10257–10274; (b) S. Basoglu, M. Yolal, A. Demirbas, H. Bektas, R. Abbasoglu and N. Demirbas, *Turk. J. Chem.*, 2013, **36**, 37–53; (c) A. Inoue, S. Miki, M. Seto, T. Kikuchi, S. Morita, H. Ueda, Y. Misu and Y. Nakata, *Eur. J. Pharmacol.*, 1997, **321**, 105–111; (d) K. Prasad, K. Srinivas, A. Pallavi and K. Mukkanti, *Drug Test. Anal.*, 2018, **10**, 212–221; (e) B. Barlaam, R. Ducray, C. Lambert-van der Brempt, P. Ple, C. Bardelle, N. Brooks, T. Coleman, D. Cross, J. G. Kettle and J. Read, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 2207–2211.

2 For aniline synthesis through copper catalyzed C–N bond formation, see: (a) S. V. Ley and A. W. Thomas, *Angew. Chem., Int. Ed.*, 2003, **42**, 5400–5449; (b) C. Sambiagio, S. P. Marsden, A. J. Blacker and P. C. McGowan, *Chem. Soc. Rev.*, 2014, **43**, 3525–3550; (c) S. Bhunia, G. G. Pawar, S. V. Kumar, Y. Jiang and D. Ma, *Angew. Chem., Int. Ed.*, 2017, **56**, 16136–16179. For aniline synthesis through nickel catalyzed C–N bond formation, see: ; (d) M. Marín, R. J. Rama and M. C. Nicasio, *Chem. Rec.*, 2016, **16**, 1819–1832. For aniline synthesis through cobalt catalyzed C–N bond formation, see: ; (e) M. Usman, Z.-H. Ren, Y.-Y. Wang and Z.-H. Guan, *Synthesis*, 2017, **49**, 1419–1443; (f) Y.-H. Chen, S. Grassl and P. Knochel, *Angew. Chem., Int. Ed.*, 2018, **57**, 1108–1111. For aniline synthesis through transition metal-free C–N bond formation, see: ; (g) C. Zhu and J. R. Falck, *Adv. Synth. Catal.*, 2014, **356**, 2395–2410.

3 (a) F. Paul, J. Patt and J. F. Hartwig, *J. Am. Chem. Soc.*, 1994, **116**, 5969–5970; (b) A. S. Guram and S. L. Buchwald, *J. Am. Chem. Soc.*, 1994, **116**, 7901–7902; (c) J. F. Hartwig, *Acc. Chem. Res.*, 2008, **41**, 1534–1544; (d) D. S. Surry and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2008, **47**, 6338–6361.

4 For seminal work, see: (a) Z. Dong and G. Dong, *J. Am. Chem. Soc.*, 2013, **135**, 18350–18353. For selected following studies, see: ; (b) Z.-Y. Chen, C.-Q. Ye, H. Zhu, X.-P. Zeng and J.-J. Yuan, *Chem.–Eur. J.*, 2014, **20**, 4237–4241; (c) P.-X. Zhou, Y.-Y. Ye, J.-W. Ma, L. Zheng, Q. Tang, Y.-F. Qiu, B. Song, Z.-H. Qiu, P.-F. Xu and Y.-M. Liang, *J. Org. Chem.*, 2014, **79**, 6627–6633; (d) F. Sun and Z. Gu, *Org. Lett.*, 2015, **17**, 2222–2225; (e) H. Shi, D. J. Babinski and T. Ritter, *J. Am. Chem. Soc.*, 2015, **137**, 3775–3778; (f) B. Luo, J.-M. Gao and M. Lautens, *Org. Lett.*, 2016, **18**, 4166–4169; (g) P. Wang, G.-C. Li, P. Jain, M. E. Farmer, J. He, P.-X. Shen and J.-Q. Yu, *J. Am. Chem. Soc.*, 2016, **138**, 14092–14099; (h) W. C. Fu, B. Zheng, Q. Zhao, W. T. K. Chan and F. Y. Kwong, *Org. Lett.*, 2017, **19**, 4335–4338; (i) L. Fan, J. Liu, L. Bai, Y. Wang and X. Luan, *Angew. Chem., Int. Ed.*, 2017, **56**, 14257–14261.

5 Z. Dong, G. Lu, J. Wang, P. Liu and G. Dong, *J. Am. Chem. Soc.*, 2018, **140**, 8551–8562.

6 For seminal work, see: (a) M. Catellani, F. Frignani and A. Rangoni, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 119–122. For selected reviews, see: ; (b) M. Catellani, *Top. Organomet. Chem.*, 2005, **14**, 21–53; (c) M. Catellani, E. Motti and N. Della Ca', *Acc. Chem. Res.*, 2008, **41**, 1512–1522; (d) J. Ye and M. Lautens, *Nat. Chem.*, 2015, **7**, 863–870; (e) N. Della Ca', M. Fontana, E. Motti and M. Catellani, *Acc. Chem. Res.*, 2016, **49**, 1389–1400; (f) Z.-S. Liu, Q. Gao, H.-G. Cheng and Q. Zhou, *Chem.–Eur. J.*, 2018, **24**, 15461–15476; (g) H.-G. Cheng, S. Chen, R. Chen and Q. Zhou, *Angew. Chem., Int. Ed.*, 2019, **58**, 5832–5844; (h) J. Wang and G. Dong, *Chem. Rev.*, 2019, **119**, 7478–7528; For selected recent studies, see: (i) Y. Yamamoto, T. Murayama, J. Jiang, T. Yasui and M. Shibuya, *Chem. Sci.*, 2018, **9**, 1191–1199; (j) Z.-S. Liu, G. Qian, Q. Gao, P. Wang, H.-G. Cheng, Q. Wei, Q. Liu and Q. Zhou, *ACS Catal.*, 2018, **8**, 4783–4788; (k) R. Li and G. Dong, *Angew. Chem., Int. Ed.*, 2018, **57**, 1697–1701; (l) Q. Zhao, W. C. Fu and F. Y. Kwong, *Angew. Chem., Int. Ed.*, 2018, **57**, 3381–3385; (m) H.-G. Cheng, C. Wu, H. Chen, R. Chen, G. Qian, Z. Geng, Q. Wei, Y. Xia, J. Zhang, Y. Zhang and Q. Zhou, *Angew. Chem., Int. Ed.*, 2018, **57**, 3444–3448; (n) L. Bai, J. Liu, W. Hu, K. Li, Y. Wang and X. Luan, *Angew. Chem., Int. Ed.*, 2018, **57**, 5151–5155; (o) G. Qian, M. Bai, S. Gao, H. Chen, S. Zhou, H.-G. Cheng, W. Yan and Q. Zhou, *Angew. Chem., Int. Ed.*, 2018, **57**, 10980–10984; (p) C. Wu, H.-G. Cheng, R. Chen, H. Chen, Z.-S. Liu, J. Zhang, Y. Zhang, Y. Zhu, Z. Geng and Q. Zhou, *Org. Chem. Front.*, 2018, **5**, 2533–2536; (q) F. Liu, Z. Dong, J. Wang and G. Dong, *Angew. Chem., Int. Ed.*, 2019, **58**, 2144–2148; (r) Q. Gao, Z.-S. Liu, Y. Hua, L. Li, H.-G. Cheng, H. Cong and Q. Zhou, *Chem. Commun.*, 2019, **55**, 8816–8819.

7 (a) G. Shi, C. Shao, X. Ma, Y. Gu and Y. Zhang, *ACS Catal.*, 2018, **8**, 3775–3779; (b) S. Chen, Z.-S. Liu, T. Yang, Y. Hua,

Z. Zhou, H.-G. Cheng and Q. Zhou, *Angew. Chem., Int. Ed.*, 2018, **57**, 7161–7165; (*c*) P. Wang, S. Chen, Z. Zhou, H.-G. Cheng and Q. Zhou, *Org. Lett.*, 2019, **21**, 3323–3327.

8 Very recently, the Dong group reported an elegant *ortho* acylation of aryl boroxines *via* palladium/norbornene cooperative catalysis, see: R. Li, F. Liu and G. Dong, *Chem*, 2019, **5**, 929–939. In their research, pinacol arylborates are unreactive substrates. They also reported the *ortho* amination of aryl boroxines (six examples), which required triphenyl phosphite as the ligand, and CsI and benzoquinone (BQ) as the additives.

9 For palladium(IV)-involved aminations, see: (*a*) J. A. Jordan-Hore, C. C. Johansson, M. Gulias, E. M. Beck and M. J. Gaunt, *J. Am. Chem. Soc.*, 2008, **130**, 16184–16186; (*b*) T. Mei, X. Wang and J.-Q. Yu, *J. Am. Chem. Soc.*, 2009, **131**, 10806–10807. However, another mechanism involving direct nucleophilic substitution of the amination reagent **2** by arylpalladium(II) species (**II**) can't be excluded, see related references: ; (*c*) A. M. Berman and J. S. Johnson, *J. Am. Chem. Soc.*, 2004, **126**, 5680–5681; (*d*) T. J. Barker and E. R. Jarvo, *J. Am. Chem. Soc.*, 2009, **131**, 15598–15599; (*e*) G. Cheng, T.-J. Li and J.-Q. Yu, *J. Am. Chem. Soc.*, 2015, **137**, 10950–10953.

10 For selected Catellani-type studies involving redox-neutral protonation as the termination step, see: (*a*) L. Jiao and T. Bach, *J. Am. Chem. Soc.*, 2011, **133**, 12990–12993; (*b*) L. Jiao, E. Herdtweck and T. Bach, *J. Am. Chem. Soc.*, 2013, **134**, 14563–14572; (*c*) X.-C. Wang, W. Gong, L.-Z. Fang, R.-Y. Zhu, S. Li, K. M. Engle and J.-Q. Yu, *Nature*, 2015, **519**, 334–338; (*d*) Z. Dong, J. Wang and G. Dong, *J. Am. Chem. Soc.*, 2015, **137**, 5887–5890; (*e*) H. Zhang, H.-Y. Wang, Y. Luo, C. Chen, Y. Cao, P. Chen, Y.-L. Guo, Y. Lan and G. Liu, *ACS Catal.*, 2018, **8**, 2173–2180. For a review about protodepalladation, see: ; (*f*) M. L. O'Duill and K. M. Engle, *Synthesis*, 2018, **50**, 4699–4714.

11 The oxidation state of the palladium complexes may be kept at two throughout the catalytic cycle. For selected examples, see: Y.-H. Zhang, B.-F. Shi and J.-Q. Yu, *Angew. Chem., Int. Ed.*, 2009, **48**, 6097–6100; and ref. 9*e*.

12 For mechanistic studies on Catellani-type reactions, see: (*a*) M. Catellani and B. E. Mann, *J. Organomet. Chem.*, 1990, **390**, 251–255; (*b*) G. Bocelli, M. Catellani and S. Ghelli, *J. Organomet. Chem.*, 1993, **458**, C12–C15; (*c*) B. Martín-Matute, C. Mateo, D. J. Cárdenas and A. M. Echavarren, *Chem.–Eur. J.*, 2001, **7**, 2341–2348; (*d*) D. J. Cárdenas, B. MartínMatute and A. M. Echavarren, *J. Am. Chem. Soc.*, 2006, **128**, 5033–5040; (*e*) G. Maestri, E. Motti, N. Della Ca', M. Malacria, E. Derat and M. Catellani, *J. Am. Chem. Soc.*, 2011, **133**, 8574–8585; (*f*) D. I. Chai, P. Thansandote and M. Lautens, *Chem.–Eur. J.*, 2011, **17**, 8175–8188.

13 (*a*) S. N. Mlynarski, A. S. Karns and J. P. Morken, *J. Am. Chem. Soc.*, 2013, **134**, 16449–16451; (*b*) C. Zhu, G. Li, D. H. Ess, J. R. Falck and L. Kürti, *J. Am. Chem. Soc.*, 2013, **134**, 18253–18256; and ref. 2*g*.

14 D. V. Partyka, *Chem. Rev.*, 2011, **111**, 1529–1595.

15 M. Kotora and T. Takahashi, in *Handbook of Organopalladium Chemistry for Organic Synthesis, Vol. 1*, ed. E.-i. Negishi, Wiley, New York, 2002, pp. 973–993.

16 J.-P. Corbet and G. Mignani, *Chem. Rev.*, 2006, **106**, 2651–2710.

17 R. D. Taylor, M. MacCoss and A. D. G. Lawson, *J. Med. Chem.*, 2014, **57**, 5845–5859.

18 C. Ye, H. Zhu and Z. Chen, *J. Org. Chem.*, 2014, **79**, 8900–8905.

19 (*a*) C. Bardelle, B. Barlaam, N. Brooks, T. Coleman, D. Cross, R. Ducray, I. Green, C. Lambert-van der Brempt, A. Olivier and J. Read, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 6242–6245; (*b*) K. Ebert, J. Wiemer, J. Caballero, M. Köckerling, J. Steinbach, J. Pietzsch and C. Mamat, *Bioorg. Med. Chem.*, 2015, **23**, 6025–6035. And ref. 1*e*.

20 (*a*) M. Fan, W. Zhou, Y. Jiang and D. Ma, *Org. Lett.*, 2015, **17**, 5934–5937; (*b*) J. Gao, S. Bhunia, K. Wang, L. Gan, S. Xia and D. Ma, *Org. Lett.*, 2017, **19**, 2809–2812.

21 For the general method for the synthesis of **8**, see: ref. 19*b*.

22 For a precedent using ethers (*e.g.* DME) as the hydride source, see: A. Martins, D. A. Candito and M. Lautens, *Org. Lett.*, 2010, **12**, 5186–5188.

23 F. Mo, J. Yan, D. Qiu, F. Li, Y. Zhang and J. Wang, *Angew. Chem., Int. Ed.*, 2010, **49**, 2028–2032.