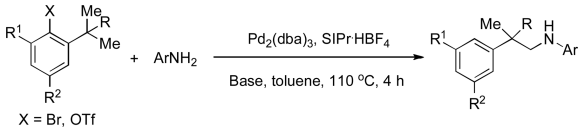
Published in final edited form as:
Angew Chem Int Ed Engl. 2011 September 5; 50(37): 8647–8651. doi:10.1002/anie.201102880.

Pd(0)-Catalyzed Intermolecular Amination of Unactivated C(sp³)–H Bonds**

Jun Pan, **Mingjuan Su**, and **Stephen L. Buchwald***
Department of Chemistry, Room 18-490, Massachusetts Institute of Technology, Cambridge, MA 02139 (USA)

Abstract

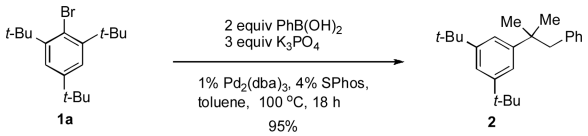


The Pd(0)-catalyzed intermolecular C–H amination of unactivated C(sp^3)–H bonds using aryl amines as the nitrogen source is disclosed. Either the C–N cross-coupling product or the C–H amination product could be accessed selectively by adjusting the steric environment of the substrate.

Keywords

C–H amination; unactivated C(sp^3)–H bonds; palladium; catalysis

Nitrogen-containing compounds are ubiquitous among biologically active molecules.[1] Consequently, the development of efficient methods to form carbon-nitrogen bonds is of great importance. From a synthetic standpoint, a strategy involving transition metal-catalyzed C–H bond activation followed by C–N bond formation represents an extremely attractive approach for installing nitrogen functional groups.[2] In fact, great achievements have been made based on amination of C(sp^2)–H bonds,[3] as well as activated C(sp^3)–H bonds.[3h, 4] However, the activation of a simple C(sp^3)–H bond followed by C–N bond formation remains a challenge, especially in an intermolecular fashion.[5] To the best of our knowledge, the intermolecular C–H amination of unactivated C(sp^3)–H bonds has only been reported using *in situ*-generated, highly reactive nitrene intermediates.[6] Thus, the development of complementary methods is strongly desired. Herein, we report on the Pd(0)-catalyzed intermolecular C–H amination of unactivated C(sp^3)–H bonds using aryl amines as the nitrogen source.



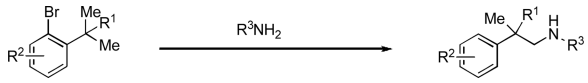
**Generous financial support from the National Institutes of Health (GM-46059) is gratefully acknowledged. The Bruker 400 MHz instrument used in this work was purchased with funding from the National Institutes of Health (GM 1S10RR13886-01). We are grateful to Georgiy Teverovskiy (MIT) for initial studies on DFT calculations and to Sophie Rousseaux (MIT) for helpful discussions.

Fax: (+1) 617-253-3297, sbuchwal@mit.edu.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

(1)

During our investigation of Suzuki-Miyaura cross-coupling processes,[7] we disclosed that the reaction of 1-bromo-2,4,6-tri-*tert*-butylbenzene **(1a)** with phenylboronic acid produced the α,α-dimethyl-β-phenyl hydrostyrene, **2**, in 95% yield, instead of the desired biaryl [Eq. (1)]. This transformation likely proceeds *via* a pathway involving a tandem C–H activation/ Suzuki-Miyaura cross-coupling reaction. On the basis of these results, we postulated that a related transformation involving an intermolecular tandem C(sp^3)–H activation/C–N coupling might be feasible [Eq. (2)].



(2)

Our study commenced by examining the C–H amination of **1a** to afford the corresponding *N*-(2-methyl-2-phenylpropyl)aniline, **3a**, using Pd catalysts based on different ligands. While the biarylphosphane ligands developed in our laboratory led to catalysts that exhibited modest activities (Table 1, entries 1 to 7),[8] an examination of alternative ligand classes revealed that the utilization of a *N*-heterocyclic carbene ligand (SIPr·HBF_4) provided a significantly improved reaction efficiency to afford **3a** in 80% yield (Table 1, entry 13).[9] Further optimization of the solvent system led to an 83% isolated yield of **3a** (Table 1, entry 14).

With optimized conditions in hand, we then evaluated the scope of the C–H amination of **1a** with respect to the aryl amine component (Table 2). Both electron-rich and electron-deficient anilines gave the expected products in good to excellent yield (**3a**–**3f**), as well as anilines containing an *ortho* alkyl substituent (**3e**). We were pleased to find that heteroaryl amines such as 3-aminopyridine and 3-aminoquinoline also provided the corresponding products in good yields (**3g, 3h**). Unfortunately, *N*-substituted anilines and alkyl amines do not work under current reaction conditions. It is worth noting that, for reactions of **1a** with aryl amines, no diaryl amines were observed despite the fact that SIPr·HBF_4 is an efficient ligand for Pd-catalyzed C–N cross-coupling reactions.[10] We reasoned that this was likely due to the steric effects of the two *ortho tert*-butyl groups of **1a**.

We next examined the reactivity of less sterically hindered substrates (Table 3). The reaction of **4a** with aniline produced the diaryl amine **4b** as the sole product (Table 3, entry 1). It is likely that the *ortho* methyl group does not possess the steric bulk necessary to suppress the direct C–N cross-coupling. Replacing the methyl group with a bulkier isopropyl, cyclopentyl or cyclohexyl group led to a complete suppression of the C–N cross-coupling pathway, affording the desired C–H amination products exclusively in 75–81% yields (Table 3, entries 2–4). No C–H amination of the isopropyl, cyclopentyl or cyclohexyl group was observed, indicating the amination is highly selective for only the methyl groups of the *tert*-butyl group. The steric influence on the outcome of this reaction could be further illustrated when using the diol-protected benzaldehyde substrates **8a**, **9a** and **10a**. In the reaction of ethylene glycol-protected substrate **8a** with aniline, only the direct C–N cross-coupling product **8b** was observed (Table 3, entry 5). However, using a more sterically hindered pinacol-protecting group led to the formation of a 1:1 ratio of the C–N cross-coupling product **9b** and the C–H amination product **9c** (Table 3, entry 6). A further increase in size of the diol-protecting group resulted in exclusive formation of the C–H amination product **10b** (Table 3, entry 7). Thus, a simple switch of diol from ethylene glycol to 2,4-dimethyl-2,4-pentanediol allows access to both the C–N cross-coupling product and the C–H amination product selectively. In addition, substrate **11a** bearing an *ortho* OTIPS group underwent the C–H amination smoothly giving the desired product **11b** in 80% yield (Table

3, entry 8). It should be noted that the reaction was not restricted to aryl bromide substrates. Starting from aryl triflate **12a**, the corresponding C–H amination product **12b** was also produced in good yield when LiO^tBu was employed as base instead of NaO^tBu (Table 3, entry 9). C–H amination of the TMS group was not observed. Employing **13a** under the optimized reaction conditions provided the desired product **13b** along with the olefin product **13c** (Table 3, entry 10). By-product **13c** possibly arose from the C–H activation of the ethyl group followed by β-H elimination.[11] Interestingly, the *tert*-amyl group in the *para* position plays a crucial role in producing the desired product, as **14a** failed to yield any C–H amination product under the same reaction conditions. Instead, a mixture of olefin **14b** and benzocyclobutene **14c**[12] was obtained in a ratio of 1:1.4 and in an 81% combined yield (Scheme 1). It is worth noting that the reactive benzylic and ethereal hydrogens are tolerated in the reaction (Table 3, entries 1 to 7). Therefore, it provides an orthogonal approach to the existing nitrene methods.[2]

Based on the results described above, we propose a reaction mechanism as shown in Scheme 2. The oxidative addition of Pd^0 to aryl bromide **15** gives intermediate **16**, which would undergo C–H activation of one of the C(sp^3)–H bonds to form palladacycle **17**. Protonation of the C(sp^2)–Pd bond of **17** affords the alkyl Pd^{II} species **18**, which then undergoes transmetallation with aniline to give **19**. Finally, reductive elimination occurs to yield the product **20** with concomitant regeneration of LPd(0). A sterically hindered R^1 group helps to suppress the direct C–N cross-coupling (side reaction **A**), as well as the benzocyclobutene formation (side reaction **B**).[12] Therefore, it diminishes the formation of undesired by-products **21** and **22**. In addition, as suggested by the results of the reaction of **14a** with aniline, a bulky R^2 group seems critical to minimize the formation of by-product **24** that most likely arises from the intramolecular C(sp^2)–H activation of **18** followed by reductive elimination (side reaction **C**).[12]

To gain additional insight into the steric influence of the substrates **8a**, **9a**, and **10a** on direct C–N cross-coupling vs. C–H amination, we performed a computational study at the density functional theory (DFT) level with the hybrid functionals B3LYP.[13] The oxidative addition intermediates of **8a, 9a** and **10a** were evaluated (Table 4). The intermediates (**OA1a, OA2a** and **OA3a**) with the carbene ligand trans to the aromatic ring are found to be more stable. The calculated distances between the Pd^{II} atom and the C–H σ bond of the *tert*-butyl group and the bond angles, Pd–C1–C2, are listed in Table 4. It is worth noting that the distance decreases as the size of diol-protecting group increases; the Pd is being "pushed" toward the *tert*-butyl group as indicated by the decrease in the bond angle. In addition, the calculated distances are consistent with a three-center two-electron, agostic interaction between the Pd^{II} atom and the C–H σ bond in **OA2a** and **OA3a**.[12, 14] As recently demonstrated,[14c, 15] an agostic interaction increases the acidity of the C–H bond that is geminal to the agostic C–H bond. This is supported by the computed natural atomic charges. For **OA3a**, the agostic hydrogen atom has a less positive charge (+0.203) than either of the geminal hydrogen atoms (+0.227 and +0.225). Similar results were found for **OA2a** (agostic H: +0.150; geminal H: +0.209, 0.211). The shorter distance in **OA3a** suggests that the agostic interaction is likely stronger than that in **OA2a**. This stronger agostic interaction in **OA3** confers a more acidic character on the geminal hydrogen atom to be deprotonated. Consequently, the tendency for the subsequent C–H activation rises from **OA1a** to **OA3a** (**OA1a** < **OA2a** < **OA3a**), which is indeed consistent with our experimental observations.

In summary, we have developed a conceptually novel Pd(0)-catalyzed intermolecular C–H amination of unactivated C(sp^3)–H bonds using aryl amines as the nitrogen source. We have also demonstrated a selective access to both the C–N cross-coupling product and the C–H amination product by adjusting the steric environment of the substrate. To the best of our knowledge, this reaction is the first intermolecular unactivated C(sp^3)–H bond activation/C–

N bond-forming process that does not involve nitrenes. Further investigations to increase the generality of this process and to better understand its mechanism are currently underway in our laboratory.

Experimental Section

Typical procedure: In a nitrogen-filled glovebox, to an oven-dried test tube containing a magnetic stir bar, was added aryl bromide (1.0 mmol, 1.0 equiv), $Pd_2(dba)_3$ (46 mg, 5 mol %), SIPr·HBF_4 (53 mg, 11 mol %), NaO*t*Bu (144 mg, 1.5 mmol, 1.5 equiv), aryl amine (1.2 mmol, 1.2 equiv) and toluene (10 mL). The test tube was sealed with a Teflon-lined septum, removed from the glovebox, and heated at 110 °C in a pre-heated oil bath for 4 h. After the reaction was complete, the reaction mixture was allowed to cool to room temperature, filtered through a plug of silica gel and eluted with diethyl ether. The filtrate was concentrated in vacuo and the crude product was purified by flash chromatography on silica gel.

Supplementary Material

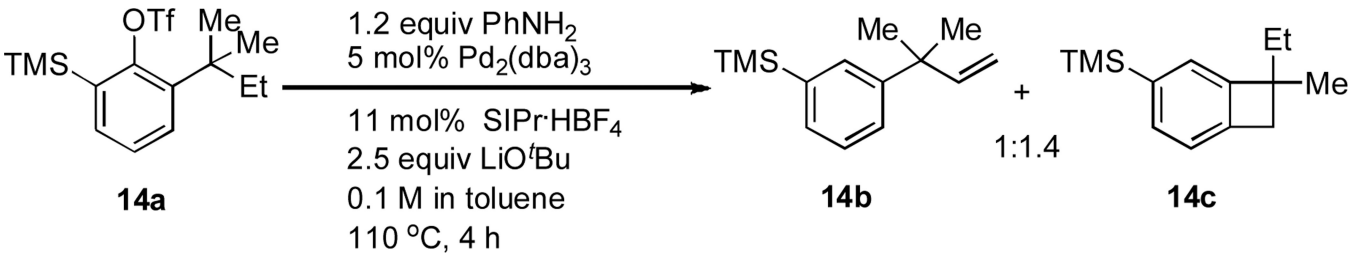
Refer to Web version on PubMed Central for supplementary material.

References

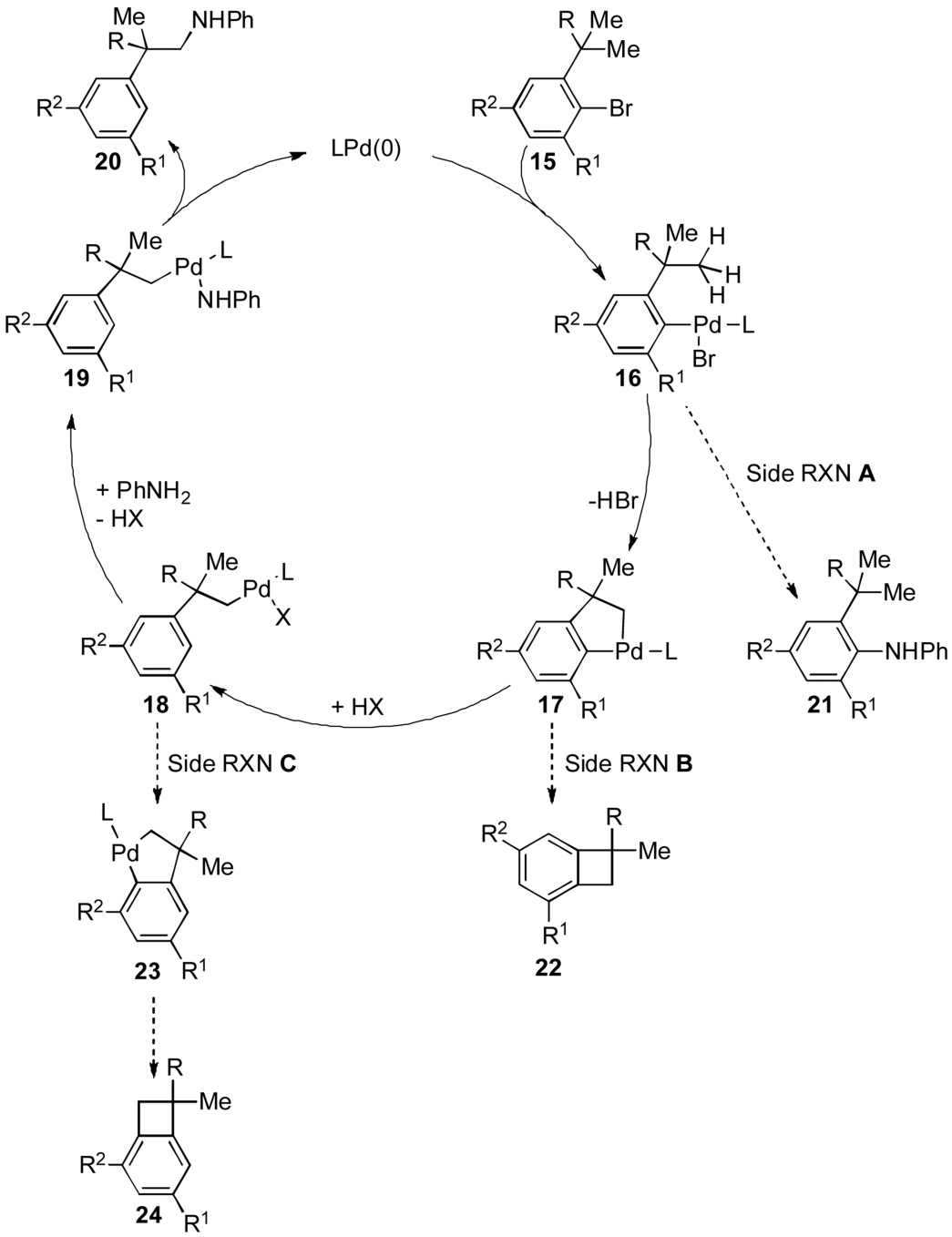
1. a) Kibayashi C. Chem. Pharm. Bull. 2005; 53:1375. [PubMed: 16272717] b) Cheng JH, Kamiya K, Kodama I. Cardiovasc. Drug Rev. 2001; 19:152. [PubMed: 11484068] c) Sanchez C, Mendez C, Salas JA. Nat. Prod. Rep. 2006; 23:1007. [PubMed: 17119643]
2. For recent reviews on C–H amination, see: Armstrong A, Collins JC. Angew. Chem. Int. Ed. 2010; 49:2282. Thansandote P, Lautens M. Chem. Eur. J. 2009; 15:5874. [PubMed: 19440997] Collet F, Dodd RH, Dauban P. Chem. Commun. 2009:5061. Davies HML, Manning JR. Nature. 2008; 451:417. [PubMed: 18216847] Dick AR, Sanford MS. Tetrahedron. 2006; 62:2439. Davies HML, Long MS. Angew. Chem. Int. Ed. 2005; 44:3518. Muller P, Fruit C. Chem. Rev. 2003; 103:2905. [PubMed: 12914485] Collet F, Lescot C, Dauban P. Chem. Soc. Rev. 2011; 40:1926. [PubMed: 21234469] Zalatan DN, Du Bois J. Top. Curr. Chem. 2010; 292:347. [PubMed: 21500412]
3. For selected examples of C–N bond formation following activation of C(sp^2)–H bonds, see: Sun K, Li Y, Xiong T, Zhang J, Zhang Q. J. Am. Chem. Soc. 2011; 133:1694. [PubMed: 21250687] Xiao B, Gong T-J, Xu J, Liu Z-J, Liu L. J. Am. Chem. Soc. 2011; 133:1466. [PubMed: 21218796] Tan YC, Hartwig JF. J. Am. Chem. Soc. 2010; 132:3676. [PubMed: 20187645] Ng KH, Chan ASC, Yu WY. J. Am. Chem. Soc. 2010; 132:12862. [PubMed: 20735142] Inamoto K, Saito T, Hiroya K, Doi T. J. Org. Chem. 2010; 75:3900. [PubMed: 20446748] Monguchi D, Fujiwara T, Furukawa H, Mori A. J. Org. Lett. 2009; 11:1607. Mei TS, Wang XS, Yu JQ. J. Am. Chem. Soc. 2009; 131:10806. [PubMed: 19606861] Wasa M, Yu JQ. J. Am. Chem. Soc. 2008; 130:14058. [PubMed: 18834119] Jordan-Hore JA, Johansson CCC, Gulias M, Beck EM, Gaunt MJ. J. Am. Chem. Soc. 2008; 130:16184. [PubMed: 18998652] Tsang WCP, Munday RH, Brasche G, Zheng N, Buchwald SL. J. Org. Chem. 2008; 73:7603. [PubMed: 18761437] Brasche G, Buchwald SL. Angew. Chem. Int. Ed. 2008; 47:1932. Chen X, Hao XS, Goodhue CE, Yu JQ. J. Am. Chem. Soc. 2006; 128:6790. [PubMed: 16719450] Tsang WCP, Zheng N, Buchwald SL. J. Am. Chem. Soc. 2005; 127:14560. [PubMed: 16231894] Wang Q, Schreiber SL. J. Org. Lett. 2009; 11:5178. Kienle M, Dunst C, Knochel P. J. Org. Lett. 2009; 11:5158. Kawano T, Hirano K, Satoh T, Miura M. J. Am. Chem. Soc. 2010; 132:6900. [PubMed: 20438076] Zhao HQ, Wang M, Su WP, Hong MC. Adv. Synth. Catal. 2010; 352:1301. Wang HG, Wang Y, Peng CL, Zhang JC, Zhu QA. J. Am. Chem. Soc. 2010; 132:13217. [PubMed: 20822153] Cho SH, Kim JY, Lee SY, Chang S. Angew. Chem. Int. Ed. 2009; 48:9127. Miyasaka M, Hirano K, Satoh T, Kowalczyk R, Bolm C, Miura M. J. Org. Lett. 2010; 13:359. Guo S, Qian B, Xie Y, Xia C, Huang H. J. Org. Lett. 2010; 13:522.
4. For selected examples of C–H amination of activated C(sp^3)–H bonds which include allylic, benzylic C–H bonds, and C–H bonds having heteroatoms or electron-withdrawing substituents on the carbon, see: Diaz-Requejo MM, Belderrain TR, Nicasio MC, Trofimenko S, Perez PJ. J. Am.

Chem. Soc. 2003; 125:12078. [PubMed: 14518978] Fructos MR, Trofimenko S, Diaz-Requejo MM, Perez PJ. J. Am. Chem. Soc. 2006; 128:11784. [PubMed: 16953617] Bhuyan R, Nicholas KM. Org. Lett. 2007; 9:3957. [PubMed: 17718576] Pelletier G, Powell DA. Org. Lett. 2006; 8:6031. [PubMed: 17165922] Liang JL, Yuan SX, Huang JS, Yu WY, Che CM. Angew. Chem. Int. Ed. 2002; 41:3465. Liang JL, Yuan SX, Huang JS, Che CM. J. Org. Chem. 2004; 69:3610. [PubMed: 15152988] Espino CG, Fiori KW, Kim M, Du Bois J. J. Am. Chem. Soc. 2004; 126:15378. [PubMed: 15563154] Fiori KW, Du Bois J. J. Am. Chem. Soc. 2007; 129:562. [PubMed: 17227019] Zhang Y, Fu H, Jiang Y, Zhao Y. J. Org. Lett. 2007; 9:3813. Milczek E, Boudet N, Blakey S. Angew. Chem. Int. Ed. 2008; 47:6825. Fraunhoffer KJ, White MC. J. Am. Chem. Soc. 2007; 129:7274. [PubMed: 17516648] Reed SA, White MC. J. Am. Chem. Soc. 2008; 130:3316. [PubMed: 18302379] Liu GS, Yin GY, Wu L. Angew. Chem. Int. Ed. 2008; 47:4733.

5. For an elegant example of intramolecular C–H amination of unactivated C(sp^3)–H bonds, see: Neumann JJ, Rakshit S, Droge T, Glorius F. Angew. Chem. Int. Ed. 2009; 48:6892.
6. a) Thu HY, Yu WY, Che CM. J. Am. Chem. Soc. 2006; 128:9048. [PubMed: 16834374] b) Li ZG, Capretto DA, Rahaman R, He CA. Angew. Chem. Int. Ed. 2007; 46:5184.c) Liang CG, Robert-Pedlard F, Fruit C, Muller P, Dodd RH, Dauban P. Angew. Chem. Int. Ed. 2006; 45:4641.d) Liang CG, Collet F, Robert-Peillard F, Muller P, Dodd RH, Dauban P. J. Am. Chem. Soc. 2008; 130:343. [PubMed: 18072775] e) Gomez-Emeterio BP, Urbano J, Diaz-Requejo MM, Perez PJ. Organometallics. 2008; 27:4126.f) Collet F, Lescot C, Liang CG, Dauban P. Dalton Trans. 2010; 39:10401. [PubMed: 20931128]
7. Barder TE, Walker SD, Martinelli JR, Buchwald SL. J. Am. Chem. Soc. 2005; 127:4685. [PubMed: 15796535]
8. For reviews on biarylphosphane ligands, see: Surry DS, Buchwald SL. Angew. Chem. Int. Ed. 2008; 47:6338. Surry DS, Buchwald SL. Chem. Sci. 2011; 2:27. [PubMed: 22432049]
9. For recent reviews on *N*-heterocyclic carbenes, see: Nolan SP. Acc. Chem. Res. 2010; 44:91. [PubMed: 21028871] Clavier H, Nolan SP. Chem. Commun. 2010; 46:841. Marion N, Nolan SP. Acc. Chem. Res. 2008; 41:1440. [PubMed: 18774825] Marion N, Diez-Gonzalez S, Nolan IP. Angew. Chem. Int. Ed. 2007; 46:2988.
10. Marion N, Navarro O, Mei J, Stevens ED, Scott NM, Nolan SP. J. Am. Chem. Soc. 2006; 128:4101. [PubMed: 16551119]
11. a) Baudoin O, Herrbach A, Gueritte F. Angew. Chem. Int. Ed. 2003; 42:5736.b) Hitce J, Retailleau P, Baudoin O. Chem. Eur. J. 2007; 13:792. [PubMed: 17044108] c) Jazzar R, Hitce J, Renaudat A, Sofack-Kreutzer J, Baudoin O. Chem. Eur. J. 2010; 16:2654. [PubMed: 20143359]
12. For a related study on benzocyclobutene formation (mechanism & scope), see: Chaumontet M, Piccardi R, Audic N, Hitce J, Peglion JL, Clot E, Baudoin O. J. Am. Chem. Soc. 2008; 130:15157. [PubMed: 18928284]
13. See the Supporting Information for details.
14. a) Brookhart M, Green MLH, Parkin G. Natl. Acad. Sci. U.S.A. 2007; 104:6908.b) Lafrance M, Gorelsky SI, Fagnou K. J. Am. Chem. Soc. 2007; 129:14570. [PubMed: 17985911] c) Rousseaux S, Davi M, Sofack-Kreutzer J, Pierre C, Kefalidis CE, Clot E, Fagnou K, Baudoin O. J. Am. Chem. Soc. 2010; 132:10706. [PubMed: 20681703]
15. a) Haller LJL, Page MJ, Macgregor SA, Mahon MF, Whittlesey MK. J. Am. Chem. Soc. 2009; 131:4604. [PubMed: 19281174] b) Kefalidis CE, Baudoin O, Clot E. Dalton Trans. 2010; 39:10528. [PubMed: 20927457]



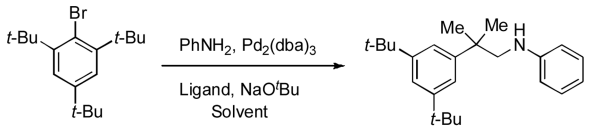
Scheme 1.
Reaction of **14a** with aniline.



Scheme 2.
Proposed mechanism of the tandem C–H activation/C–N cross-coupling.

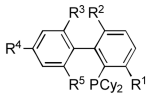
Table 1

Ligand Evaluation.[a], [b]



1a **3a**

Entry	Ligand	Yield [%][e]	Entry	Ligand	Yield [%][e]
1	XPhos	30	8[c]	$PCy_3 \cdot HBF_4$	0
2	SPhos	23	9[c]	$P^tBu_3 \cdot HBF_4$	59
3	RuPhos	32	10[c]	IMes·HCl	0
4	DavePhos	7	11[c]	IPr·HCl	30[f]
5	CPhos	23	12[c]	SIPr·HCl	72
6	BrettPhos	0	13[c]	$SIPr \cdot HBF_4$	86 (80)
7	Cy-JohnPhos	0	14[d]	$SIPr \cdot HBF_4$	88 (83)



XPhos: $R^1=R^2=H$, $R^3=R^4=R^5=^iPr$

SPhos: $R^1=R^2=R^4=H$, $R^3=R^5=OMe$

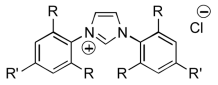
RuPhos: $R^1=R^2=R^4=H$, $R^3=R^5=O^iPr$

DavePhos: $R^1=R^2=R^3=R^4=H$, $R^5=NMe_2$

CPhos: $R^1=R^2=R^4=H$, $R^3=R^5=NMe_2$

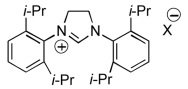
BrettPhos: $R^1=R^2=OMe$, $R^3=R^4=R^5=^iPr$

Cy-JohnPhos: $R^1=R^2=R^3=R^4=R^5=H$



IMes·HCl: R=R'=Me

IPr·HCl: R=^{i}Pr, R'=H



SIPr·HCl: X=Cl

$SIPr \cdot HBF_4$: X=BF_4

[a]Reaction conditions: **1a** (0.5 mmol), $PhNH_2$ (0.6 mmol), NaO^tBu (0.75 mmol), $Pd_2(dba)_3$ (5 mol %), ligand (20 mol %), dioxane (5 mL), 120 °C, 40 h.

[b]The reaction reached 100 % conversion, unless otherwise noted. The mass balance consists of product, reduced starting material and benzocyclobutene byproduct.

[c]Reaction was run at 110 °C for 12 h.

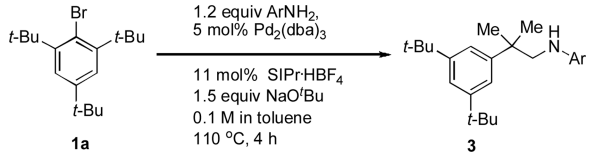
[d]Reaction was performed in toluene with 11 mol % ligand at 110 °C for 4 h.

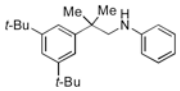
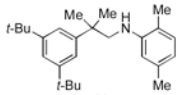
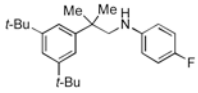
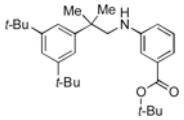
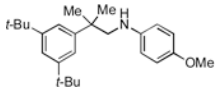
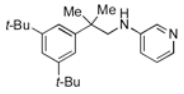
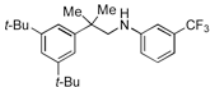
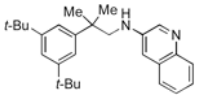
[e] Determined by GC, with dodecane as an internal standard. Yield of isolated **3a** (1 mmol scale reaction) in parentheses.

[f] The reaction reached 58 % conversion.

Table 2

C–H Amination of **1a** with Aryl Amines.[a]



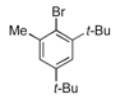
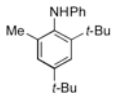
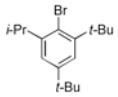
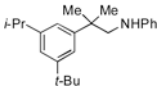
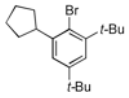
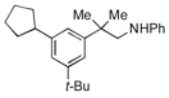
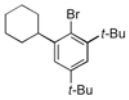
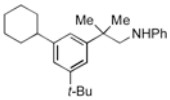
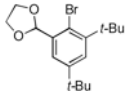
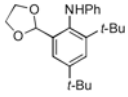
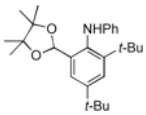
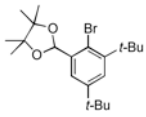
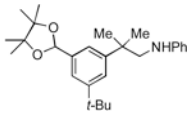
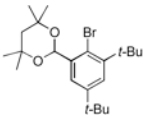
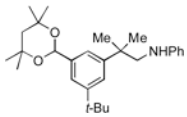
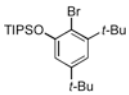
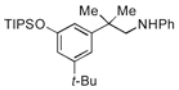
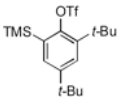
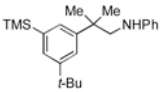
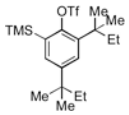
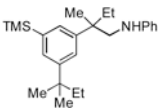
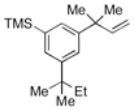
Product	Yield [%][b]	Product	Yield [%][b]
	**3a**, 83%		**3e**, 76%
	**3b**, 84%		**3f**, 76%
	**3c**, 86%		**3g**, 75%
	**3d**, 73%		**3h**, 84%

[a]Reaction conditions: **1a** (1.0 mmol), $ArNH_2$ (1.2 mmol), NaO^{t}Bu (1.5 mmol), $Pd_2(dba)_3$ (5 mol %), SIPr·HBF_4 (11 mol %), toluene (10 mL), 110 °C, 4 h.

[b]Isolated yield based on an average of two runs.

Table 3

Amination of Unactivated C(sp^3)–H Bonds with Aniline.[a]

Entry	Substrate		Product	Yield [%][b]
1		**4a**		**4b**, 94%
2		**5a**		**5b**, 75%
3		**6a**		**6b**, 77%
4		**7a**		**7b**, 81%
5		**8a**		**8b**, 82%
6		**9a**	 	**9b**, 40% **9c**, 41%
7		**10a**		**10b**, 70%
8		**11a**		**11b**, 80%
9[c]		**12a**		**12b**, 70%
10[c]		**13a**	 	**13b**, 37% **13c**, 35%

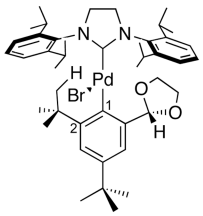
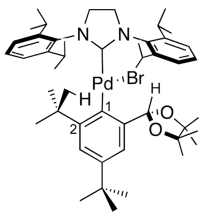
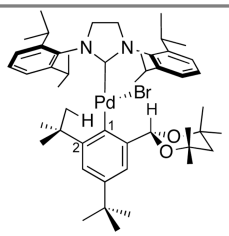
[a]Reaction conditions: substrate (1.0 mmol), $PhNH_2$ (1.2 mmol), NaO^{t}Bu (1.5 mmol), $Pd_2(dba)_3$ (5 mol %), SIPr·HBF_4 (11 mol %), toluene (10 mL), 110 °C, 4 h.

[b]Isolated yield based on an average of two runs.

[c] LiO^{t}Bu (2.5 mmol) was used.

Table 4

DFT Calculations of the Oxidative Addition Intermediates

			
	OA1a	**OA2a**	**OA3a**
Pd---C(H) (Å)	2.962	2.480	2.277
Pd–C1–C2 (°)	134.7	119.4	116.9