Synthesis of 2-Arylindoles by Suzuki Coupling Reaction of 3-Bromoindoles with Hindered Benzoboronic Acids

Guizhou Yue, Yao Wu, Caimei Wu, Zhongqiong Yin, Huabao Chen, Xianxiang Wang, Zuming Zhang

PII: S0040-4039(17)30026-6
DOI: http://dx.doi.org/10.1016/j.tetlet.2017.01.014
Reference: TETL 48517

To appear in: *Tetrahedron Letters*

Received Date: 29 October 2016
Revised Date: 3 January 2017
Accepted Date: 4 January 2017

Please cite this article as: Yue, G., Wu, Y., Wu, C., Yin, Z., Chen, H., Wang, X., Zhang, Z., Synthesis of 2-Arylindoles by Suzuki Coupling Reaction of 3-Bromoindoles with Hindered Benzoboronic Acids, *Tetrahedron Letters* (2017), doi: http://dx.doi.org/10.1016/j.tetlet.2017.01.014

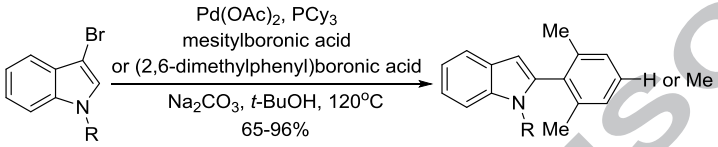
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

Synthesis of 2-Arylindoles by Suzuki Coupling Reaction of 3-Bromoindoles with Hindered Benzoboronic Acids

Leave this area blank for abstract info.

Guizhou Yue, Yao Wu, Caimei Wu, Zhongqiong Yin, Huabao Chen, Xianxiang Wang, Zuming Zhang



Tetrahedron Letters
journal homepage: www.elsevier.com

Synthesis of 2-Arylindoles by Suzuki Coupling Reaction of 3-Bromoindoles with Hindered Benzoboronic Acids

Guizhou Yue[a,b,*], Yao Wu[a], Caimei Wu[c], Zhongqiong Yin[d], Huabao Chen[b], Xianxiang Wang[a], Zuming Zhang[a]

[a]*College of Science, Sichuan Agricultural University, Ya'an, Sichuan, 625014, China*
[b]*College of Agricultural Sciences, Sichuan Agricultural University, Chengdu, Sichuan, 611130, China*
[c]*Animal Nutrition Institute, Sichuan Agricultural University, Chengdu, 611130, China*
[d]*College of Veterinary Medicine, Sichuan Agricultural University, Chengdu, Sichuan, 611130, China*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Suzuki coupling
1,2-migration
Indole
Palladium catatlysis
Boronic acid

ABSTRACT

A new synthetic method for 2-arylindoles has been developed, the process through Suzuki coupling reaction of 3-bromoindoles with hindered boronic acid catalyzed by $Pd(OAc)_2/PCy_3$, and a series of 2-arylindoles have been synthesized in moderate to high yields.

Introduction

Suzuki coupling reaction had been widely developed in academic and industrial fields, since it was found in 1979.[1] Among the numerous cross-coupling methods to construct biaryl or substituted aromatic compounds, Suzuki coupling is one of the most efficient and useful methods.[2] Suzuki coupling has several advantages, such as commercial availablility of most of boronic acids and their esters, stability of boron reagents to heat, air, and moisture, tolerance to a broad range of functional groups, low toxicity, mild reaction conditions, as well as easy separation of formed inorganic boron. Coupling of heteroaryl halides is generally considered to be more challenging than aryl ones. In particular, nitrogen-containing heterocycles, for instance, pyridine, indole and quinoline, can displace some phosphine ligands on Pd(II) complexes. In the past three decades, Buchwald phoshines,[3] bukly trialkylphosphines,[4] and other dialkylarylphosphines[5] had been exploited successfully for Suzuki coupling of heteroaryl halides.

Indole nucleus is an important motif of a huge number of biologically active alkaloids and unnatural coupounds, for example, dragmacidin D (**I**) of antiviral activity against HSV-1[6] (Figure 1), isatisine A for anti-HIV activity,[7] dimeric epipolythiodiketopiperazine alkaloids as potent anticancer reagents,[8] and compound **II** as a powerful KDR kinase inhibitor.[9] In many synthetic methods and application of indole ring,[10] palladium-catalyzed one had been researched widely and thoroughly.[11] Several elegant works for synthesis of 2-subsitituted indoles,[12] but the synthesis of 2-mesity or (2,6-dimethyl)phenylindole derivatives is rarely reported.

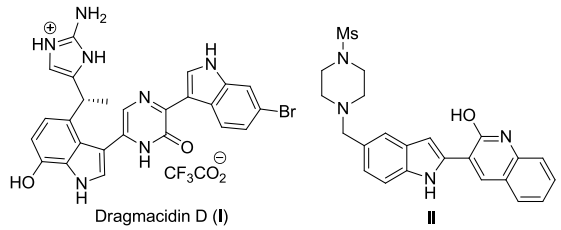
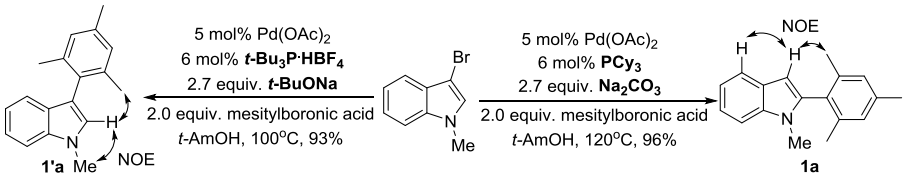


Figure 1. Selective indole alkaloids.

Recently, Zhou's group has reported the coupling of heteroaryl chlorides or bromides with aryl or heteroaryl boranes in the mild conditions[13]. In our case, 3-bromo-*N*-methylindole reacted with mesitylboronic acid[14] using $Pd(OAc)_2$ as a catalyst, we found that the product was 3-mesityl-*N*-methylindole (**1'a**) in 93% yield using *t*-

* Corresponding author. Tel.: +(86) 0835 2886189; e-mail: yueguizhou@sicau.edu.cn



Scheme 1. Synthesis of 2-mesityl-*N*-methylinodle and 3-mesityl-*N*-methylindole from 3-bromo-*N*-methylindole.

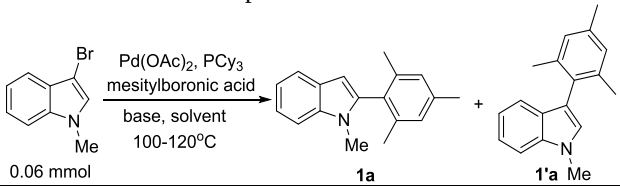
$Bu_3P•HBF_4$ as ligand and *t*-BuONa as base, whereas the employment of Cy_3P and K_2CO_3 led to 2-mesityl-*N*-methylindole (**1a**) as a single product in 96% GC yield via 1,2-migration of Pd intermediate (Scheme 1). The relative configuration of these products was confirmed easily by ^{1}H NMR spectroscopy. The C_3-H shift of indole cycle is 6.34 ppm, while the C_2-H one is 6.88 ppm. The 1D NOE and ^{1}H-^{1}H COSY experiments also unambiguously confirmed the regioselectivity of coupling reaction. To the best of our knowledge, this represents the first synthesis of 2-arylindoles through Pd-catalytic 1,2-migration. Herein, we reported the our preliminary results on this Suzuki coupling under $Pd(OAc)_2/Cy_3P$ catalytic system.

Results and Discussion

We chose 3-bromo-*N*-methylindole and mesitylboronic acid as model substrates to search for the reaction to find the optimized condition (Table 1). Initially we tested the model reaction by using 5 mol% $Pd(OAc)_2$ and 6 mmol% Cy_3P loadings when *t*-BuOK was used in tertiary amyl alcohol (*t*-AmOH) at 120°C for 24h, which gave high conversion (100 %), but very low yield (Table 1, Entry 1). As shown in Table 1, the product is almost 2-substituted indole in about 3% yield. *t*-BuONa as the base delivered 2-substituted product in 26% yield. Decreasing temperature (100°C) and shorting time (6h) could enhance yield, but the selectivity was limited. The solvent was changed to *t*-BuOH showed the same result. Other strong base, for example, CsOH and KOH, were less active. Based on the above experiments, it can be determined that the selectivity and yield were almost affected by the basicity of base. Weaker base gave better selectivity and higher yields. Na_2CO_3 showed the best result that the product was almost 2-mesityl-*N*-methylindole (Table 1, Entry 15 and 16). Furthermore, the reaction in *t*-BuOH showed a slightly higher yield than *t*-AmOH.

The steric hinderance of boronic acids were very important for the 1,2-migration of the reaction. When the mesitylboronic acid was replaced by less hindered boronic acids, for example, $PhB(OH)_2$, the product was 3-subsituted indole and not 2-subsittuted one at all. Other palladium salts, such as $Pd(PPh_3)_4$, $PdCl_2$, $Pd_2(dba)_3$ were not so efficient catalysts compared with $Pd(OAc)_2$. When the loadings of Pd salt and ligand (2.5 mmol% Pd and 3.0 mmol% Cy_3P) were decreased, the reaction had low yield. Finally, the optimal reaction condition for this Suzuki coupling was established [3-bromo-*N*-methylindole (1.0 equiv.) mesitylboronic acid (2.0 equiv.), and Na_2CO_3 (2.7 equiv.) in *t*-BuOH at 120 °C under catalyst $Pd(OAc)_2$ (5 mol%) and Cy_3P (6 mol%)].

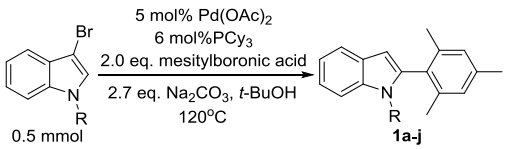
Table 1. The condition optimization of model reaction.[15]

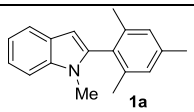
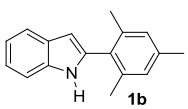
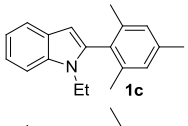
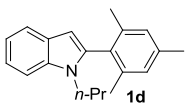
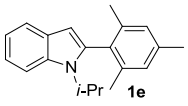
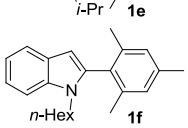


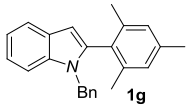
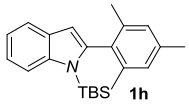
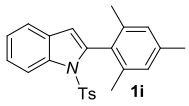
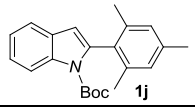
Entry	Change of conditions	GC Conversion (%)	GC Yield (%) **1a**+**1'a**
1	*t*-BuOK/*t*-AmOH/120°C/24h	100	0.2+3.4
2	*t*-BuOK/*t*-BuOH/120°C/24h	100	0+26
3	*t*-BuONa/*t*-AmOH/100°C/6h	93	13+6
4	*t*-BuONa/*t*-BuOH/100°C/6h	100	0+32
5	CsOH•H_2O/*t*-AmOH/120°C /24h	86	0.5+3
6	CsOH•H_2O/*t*-BuOH/120°C /24h	69	0.4+21
7	KOH/*t*-AmOH/100°C/6h	85	11+3
8	KOH/*t*-BuOH/100°C/6h	67	4+32
9	Cs_2CO_3/*t*-AmOH/120°C/24h	99	32+2
10	Cs_2CO_3/*t*-BuOH/120°C/24h	96	25+34
11	K_3PO_4/*t*-AmOH/120°C/24h	100	64+0
12	K_3PO_4/*t*-BuOH/120°C/24h	100	73+3
13	K_2CO_3/*t*-AmOH/100°C/6h	100	77+0.1
14	K_2CO_3/*t*-BuOH/100°C/6h	100	90+1
15	Na_2CO_3/*t*-AmOH/120°C/24h	99	96+0
16	**Na_2CO_3/*t*-BuOH/120°C/24h**	**100**	**99+0**

With the optimized conditions in hand, the scope of the reaction with 3-bromo-*N*-subsitutedindoles bearing either electron-donating or electron-withdrawing groups (Table 2) was explored. As shown in Table 2, when the substituted groups in nitrogen atom were electron-donating groups (Et, Pr, Hex, TBS, Bn etc.), the results of the reaction were good and the yields exceeded 70%. It is noted that the 3-bromo-*N*-alkylindoles, especially propyl or hexyl, were found to be very unstable to decompose in air and at the normal ambient temperature, in which probably resulted in decreased yields. The solution of 3-bromo-*N*-alkylindoles in *t*-AmOH or *t*-BuOH was found to be relatively stable in low temperature, which can partially avoid this problem. When the substituted groups were electron-withdrawing ones, the reaction was slowly and the by-product also occurred. For example, compound **1i** was partly taken off *p*-toluene sulfonyl (Ts) to obtain **1b** under the reaction condition (Table 2, Entry 9).

Table 2. Synthesis of 1-substituted-2-mesitylindole derivatives **1a-1j**[16]

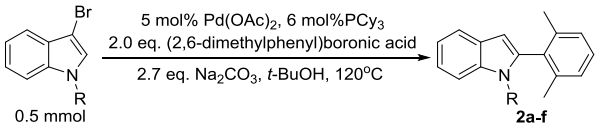


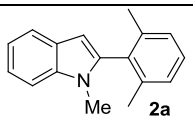
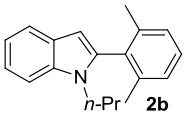
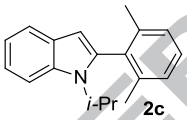
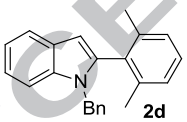
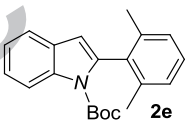
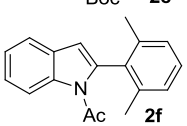
Entry	Products	Isolated Yield (%)
1	 **1a**	96
2	 **1b**	71
3	 **1c**	90
4	 **1d**	85
5	 **1e**	83
6	 **1f**	73

7		70
8		71
9		65
10		68

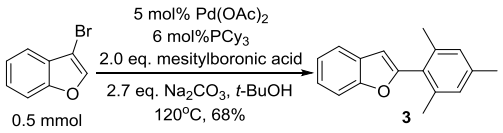
The coupling efficiency of hindered boronic acid was further examined. The reaction of 2,6-dimethylphenyl boronic acid with the above six 3-bromo-N-subsitutedindoles had been carried out (Table 3). The reaction also gave the same result and provided good to excellent yields, whether electron-withdrawing or electron-donoring groups of nitrogen atom.

Table 3. Synthesis of 1-substituted -2-(2,6-dimethylphenyl) indole derivatives **2a**-**f**[16]



Entry	Products	Isolated Yields (%)
1		90
2		82
3		76
4		70
5		70
6		66

The catalyst was also applied to other aromatic heterocycle. The reaction of 3-bromobenzofuran[17] with mesitylboronic acid smoothly proceeded under the optimized condition, which obtained **3** in 68% yield (Scheme 2). The ^{1}H and ^{13}C NMR of **3** was in agreement with the literatures[18].



Scheme 2. Synthesis of 2-mesitylbenzofuran **3**.

The mechanism of 1,2-aryl migration of indole mainly focused on the direct C-H activation by palladium-catalyzed, in which presented that features an electrophilic palladium, accompanied by a 1,2-migration of an intermediate palladium species.[12e,19] Unlike the above mechanism, we proposed mechanism of our Suzuki coupling which is shown in Figure 2. The first step of catalytic cycle involves formation of an aryl-palladium (II) intermediate (**A**) via the oxidative addition of substrate to a palladium (0) species formed *in situ*. Next, intermediate **A** is converted into the four-coordinate species (**B**) via the "oxo-palladium" pathway[2m] and transmatalation. The effect of the aryl steric hindrance and ligand compels the intermediate **B** to proceed a 1,2-migration, which generates thermodynamically more stable 2-palladium species (**C**)[20]. Finally, the reductive elimination of this species provides the 1,2-migrated products and Pd(0) species.

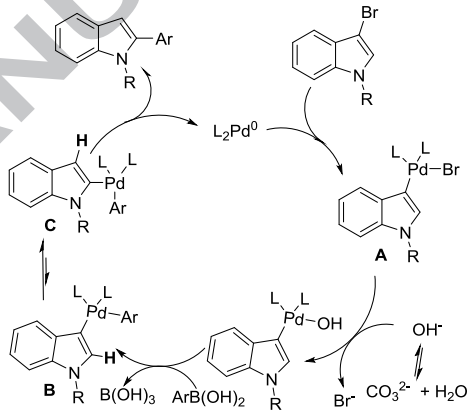


Figure 2. Proposed Catalytic Cycle.

Conclusion

A highly efficient catalytic system for direct C-2 arylation of indoles has been developed. This process involves Suzuki coupling reaction of 3-bromoindoles with hindered boronic acids and furnished sixteen 2-substitutedindole derivatives with good to excellent yields. Further exploration and application of this reaction in organic synthesis is ongoing in our laboratory.

Supporting Information for this article is available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000083.

Acknowledgments

We thank the Science & Technology Department of Sichuan Province (2012JY0118) and Sichuan Agricultural University for the financial support. We also acknowledge Prof. (Steve) Zhou of Nanyang Technological University for the helpful suggestion and discussion.

References and notes

1. Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *20*, 3437–3440.
2. (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483. (b) Suzuki, A.; Brown, H. C. *Organic Syntheses via Boranes: Suzuki Coupling*, Aldrich Chemical Company, **2003**. (c) Zhou S. L.; Xu L.

W.; Xia, C. G.; Li J. W.; Li F. W. *Chin. J. Org. Chem.* **2004**, *24*, 1501–1512. (d) Bai, L.; Wang, J.-X. *Curr. Org. Chem.* **2005**, *9*, 535–553. (e) Gracias, V.; Iyengar, R. *Chemtracts* **2005**, *18*, 339–348. (f) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275–286. (g) Weng, Z.; Teo, S.; Hor, T. A. *Acc. Chem. Res.* **2007**, *40*, 676–684. (h) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461–1473. (i) Suzuki, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 6722–6737. (j) Fihri, A.; Bouhrara, M.; Nekoueishahraki, B.; Basset, J.-M.; Polshettiwar, V. *Chem. Soc. Rev.* **2011**, *40*, 5181–5203. (k) Mora, M.; Jimenez-Sanchidrian, C.; Rafael Ruiz, J. *Curr. Org. Chem.* **2012**, *16*, 1128–1150. (l) Heravi, M. M.; Hashemi, E. *Monatsh. Chem.* **2012**, *143*, 861–880. (m) Lennox, A. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2013**, *52*, 7362–7370. (n) García-Melchor, M.; Braga, A. A.; Lledós, A.; Ujaque, G.; Maseras, F. *Acc. Chem. Res.* **2013**, *46*, 2626–2634. (o) Han, F.-S. *Chem. Soc. Rev.* **2013**, *42*, 5270–5298. (p) Kumar, A.; Rao, G. K.; Kumar, S.; Singh, A. K. *Dalton Trans.* **2013**, *42*, 5200–5223. (q) Blangetti, M.; Rosso, H.; Prandi, C.; Deagostino, A.; Venturello, P. *Molecules* **2013**, *18*, 1188–1213. (r) Hussain, I; Capricho, J.; Yawer, M. A. *Adv. Synth. Catal.* **2016**, 358, in press.

3. (a) Billingsley, K. L.; Anderson, K. W.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2006**, *45*, 3484–3488. (b) Billingsley, K.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3358–3366. (c) Knapp, D. M.; Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2009**, *131*, 6961–6963. (d) Molander, G. A.; Canturk, B.; Kennedy, L. E. *J. Org. Chem.* **2009**, *74*, 973–980.
4. (a) Kudo, N.; Perseghini, M.; Fu, G. C. *Angew. Chem. Int. Ed.* **2006**, *45*, 1282–1284. (b) Fleckenstein, C. A.; Plenio, H. *J. Org. Chem.* **2008**, *73*, 3236–3244. (c) Fleckenstein, C. A.; Plenio, H. *Chem. Eur. J.* **2008**, *14*, 4267–4279.
5. (a) Guram, A. S.; King, A. O.; Allen, J. G.; Wang, X.; Schenkel, L. B.; Chan, J.; Bunel, E. E.; Faul, M. M.; Larsen, R. D.; Martinelli, M. J. *Org. Lett.* **2006**, *8*, 1787–1789. (b) Guram, A. S.; Wang, X.; Bunel, E. E.; Faul, M. M.; Larsen, R. D.; Martinelli, M. J. *J. Org. Chem.* **2007**, *72*, 5104–5112. (c) So, C. M.; Yeung, C. C.; Lau, C. P.; Kwong, F. Y. *J. Org. Chem.* **2008**, *73*, 7803–7806. (d) So, C. M.; Lau, C. P.; Kwong, F. Y. *Org. Lett.* **2007**, *9*, 2795–2798.
6. (a) Kohmoto, S.; Kashman, Y.; McConnell, O. J.; Rinehart Jr, K. L.; Wright, A.; Koehn, F. *J. Org. Chem.* **1988**, *53*, 3116–3118. (b) Cutignano, A.; Bifulco, G.; Bruno, I.; Casapullo, A.; Gomez-Paloma, L.; Riccio, R. *Tetrahedron* **2000**, *56*, 3743–3748.
7. Liu, J.-F.; Jiang, Z.-Y.; Wang, R.-R.; Zheng, Y.-T.; Chen, J.-J.; Zhang, X.-M.; Ma, Y.-B. *Org. Lett.* **2007**, *9*, 4127–4129.
8. Kim, J.; Movassaghi, M. *Acc. Chem. Res.* **2015**, *48*, 1159–1171.
9. Fraley, M. E.; Hoffman, W. F.; Arrington, K. L.; Hungate, R. W.; Hartman, G. D.; McFall, R. C.; Coll, K. E.; Rickert, K.; Thomas, K. A.; McGaughey, G. B. *Curr. Med. Chem.* **2004**, *11*, 709–719.
10. (a) Joule, J. A. *Sci. Synth.* **2001**, *10*, 361–365. (b) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875–2911. (c) Dalpozzo, R. *Chem. Soc. Rev.* **2015**, *44*, 742–778.
11. (a) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873–2920. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644–4680.
12. See a review: Sandtorv, A. H. *Adv. Syn. Catal.* **2015**, *357*, 2403–2435. For recent examples: (a) Hamel, P.; Zajac, N.; Atkinson, J. G.; Girard, Y. *J. Org. Chem.* **1994**, *59*, 6372–6377. (b) Macleod, C.; McKiernan, G. J.; Guthrie, E. J.; Farrugia, L. J.; Hamprecht, D. W.; Macritchie, J.; Hartley, R. C. *J. Org. Chem.* **2003**, *68*, 387–401. (c) Lane, B. S.; Sames, D. *Org. Lett.* **2004**, *6*, 2897–2900. (d) Denmark, S. E.; Baird, J. D. *Org. Lett.* **2004**, *6*, 3649–3652. (e) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050–8057. (f) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972–4973. (g) Oskooie, H. A.; Heravi, M. M.; Behbahani, F. K. *Molecules* **2007**, *12*, 1438–1446. (h) Lebrasseur, N.; Larrosa, I. *J. Am. Chem. Soc.* **2008**, *130*, 2926–2927. (i) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172–8174. (j) Nandurkar, N. S.; Bhanushali, M. J.; Bhor, M. D.; Bhanage, B. M. *Tetrahedron Lett.* **2008**, *49*, 1045–1048. (k) Zhao, J.; Zhang, Y.; Cheng, K. *J. Org. Chem.* **2008**, *73*, 7428–7431. (l) Liang, Z.; Yao, B.; Zhang, Y. *Org. Lett.* **2010**, *12*, 3185–3187. (m) Alsabeh, P. G.; Lundgren, R. J.; Longobardi, L. E.; Stradiotto, M. *Chem. Commun.* **2011**, *47*, 6936–6938. (n) Huang, Y.; Lin, Z.; Cao, R. *Chem. Eur. J.* **2011**, *17*, 12706–12712. (o) Jadhav, J.; Gaikwad, V.; Kurane, R.; Salunkhe, R.; Rashinkar, G. *Synlett* **2012**, *23*, 2511–2515. (p) Feng, J.; Lu, G.; Lv, M.; Cai, C. *J. Organomet. Chem.* **2014**, *761*, 28–31. (q) Malmgren, J.; Nagendiran, A.; Tai, C. W.; Bäckvall, J. E.; Olofsson, B. *Chem. Eur. J.* **2014**, *20*, 13531–13535. (r) Lee, P.-S.; Yoshikai, N. *Org. Lett.* **2015**, *17*, 22–25. (s) Zhang, H.-J.; Wu, Z.; Lin, W.; Wen, T.-B. *Chin. J. Chem.* **2015**, *33*, 517–521. (t) Moriyama, K.; Ishida, K.; Togo, H. *Chem. Commun.* **2015**, *51*, 2273–2276. (u) Gemoets, H; Kalvet, I.; Nyuchev, A. V.; Erdmann, N.; Hessel, V.; Schoenebeck, F.; Noël T. *Chem. Sci.* **2016**, 7, in press.
13. (a) Yang, J.; Liu, S.; Zheng, J. F.; Zhou, J. S. *Eur. J. Org. Chem.* **2012**, *2012*, 6248–6259. (b) Zou, Y.; Yue, G.; Xu, J.; Zhou, J. S. *Eur. J. Org. Chem.* **2014**, *2014*, 5901–5905.
14. Recent examples for mesitylboronic acid: (a) Watanabe, T.; Miyaura, N.; Suzuki, A. *Synlett* **1992**, 207–210. (b) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020–4028. (c) Yamaguchi, K.; Yamaguchi, J.; Studer, A.; Itami, K. *Chem. Sci.* **2012**, *3*, 2165–2169. (d) Yamaguchi, K.; Kondo, H.; Yamaguchi, J.; Itami, K. *Chem. Sci.* **2013**, *4*, 3753–3757.
15. **General procedure for condition optimization:** In an argon-filled glove box, $Pd(OAc)_2$ (0.7 mg, 0.003 mmol), PCy_3(1.0 mg, 0.0036 mmol), solvent (0.4 mL) and *n*-dodecane (5 μL) were charged into a 10-mL reaction tube. After stirring for 15 min, boronic acid (0.12 mmol), base (0.162 mmol) and bromide (0.06 mmol) were added successively. The mixture was vigorously stirred in a preheated oil bath at 100 ^{o}C for 6 h and at 120 ^{o}C for 24h. At intervals, an aliquot of the reaction mixture was taken and passed through a short plug of silical gel with diethyl ether washing. The filtrates were subjected to GC analysis to determine the conversion of the organic bromides and yield of the Suzuki products.
16. **Typical procedure for Suzuki coupling reactions**: In an argon-filled glove box, to a 25 mL Schlenk tube was charged sequentially $Pd(OAc)_2$ (5.6 mg, 0.025 mmol) and PCy_3 (8.4 mg, 0.03 mmol), *t*-BuOH (2.8 mL) and *n*-dodecane (20 μL). After stirring for 15 min, mesitylboronic acid or (2, 6-dimethylphenyl) boronic acid (164 mg, 1.0 mmol), Na_2CO_3 (143 mg, 1.35 mmol) and 3-bromo-*N*-methyl indole (105 mg, 0.5 mmol) or a solution of 3-bromo-*N*-alkylindole (105 mg, 0.5 mmol) in *t*-BuOH were added. The mixture was vigorously stirred in a pre-warmed oil bath at 120 ^{o}C until the starting material was almost fully comsumed (monitored by GC or TLC). At the end of the reaction, the mixture was cooled to room temperature and added 10 mL H_2O. The aqueous phase was further extracted with Et_2O (10 mL×3). The combined organic layers were dried over Mg_2SO_4, and then concentrated on a rotary evaporator. The residue was purified by silica gel flash chromatography to obtain the desired coupling product. **1a**: ^{1}H NMR (500 MHz): δ = 7.64 (d, *J* = 7.5 Hz, 1 H), 7.35 (d, *J* = 8.0 Hz, 1 H), 7.25-7.21 (m, 1 H), 7.15-7.12 (m, 1 H), 6.98 (s, 2 H), 6.34 (s, 1 H), 3.42 (s, 3 H), 2.36 (s, 3 H), 2.03 (s, 6 H). ^{13}C MR (125 MHz): δ = 139.1, 138.6, 138.3, 137.0, 129.3, 128.3, 128.0, 120.8, 120.3, 119.3, 109.3, 100.9, 29.6, 21.14, 20.2. GC-MS (EI): Calcd for $C_{18}H_{19}N$ M^+: 249.1. Found: 249.1.
17. Kato, S.-i.; Furuya, T.; Nitani, M.; Hasebe, N.; Ie, Y.; Aso, Y.; Yoshihara, T.; Tobita, S.; Nakamura, Y. *Chem. Eur. J.* **2015**, *21*, 3115–3128.
18. (a) Yamaguchi, K.; Yamaguchi, J.; Studer, A.; Itami, K. *Chem. Sci.* **2012**, *3*, 2165–2169. (b) Chen, C.-Y.; Dormer, P. G. *J. Org. Chem.* **2005**, *70*, 6964–6967.
19. (a) Bhunia K. S.; Polley, A.; Natarajan, R.; Jana, R. *Chem. Eur. J.* **2015**, 21, 16786–16791. (b) Mochida, K.; Shimizu, M.; Hiyama, T. *J. Am. Chem. Soc.* **2009,** *131*, 8350–8351. (c) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007,** *36*, 1173–1193 and references here cited.
20. Saulnier, M. G.; Gribble, G. W. *J. Org. Chem.* **1982**, 47, 757–761.

Supplementary Material

Supplementary material (general experimental details, lists of spectral data, copies of ^{1}H and ^{13}C NMR spectra for all compounds) can be found in the online version of this article.

Highlights

1. A highly efficient catalytic system [$Pd(OAc)_2/PCy_3$] has been developed.
2. All target products were obtained with good to excellent yields.
3. The synthesis of 2-arylindole via Pd-catlytic 1, 2-migration was firstly discovered.
4. The catalyst has been also applied to synthesize 2-arylbenzofuran.