Organic LETTERS

Letter

pubs.acs.org/OrgLett

Rapid Synthesis of 3,3′ Bis-Arylated BINOL Derivatives Using a C−H Borylation *in Situ* Suzuki−Miyaura Coupling Sequence

Ijaz Ahmed and Daniel A. Clark*,†

Department of Chemistry, 1-014 Center for Science and Technology, Syracuse University, Syracuse, New York 13244, United States

Supporting Information

ABSTRACT: The increased interest in BINOL derived catalysts for asymmetric transformations has encouraged us to disclose a rapid and scalable method of preparing 3,3′ bis-arylated BINOL derivatives **1** using a one-pot CH borylation/Suzuki−Miyaura coupling sequence. The use of an aldehyde additive was found to be crucial to the success of this *in situ* tandem approach. This method was applied to the preparation of 10 BINOL derivatives, each completed within 24 h. Notably, this approach requires only a single purification step.

Over the past century, studies toward efficient asymmetric catalytic methods have been aggressively undertaken.[1] Chiral binaphthol (BINOL) derivatives have become beneficial due to their use in asymmetric Brønsted acid catalysis.[2] Notably, 3,3′ bis-arylated BINOL derivatives **1** are valuable precursors for an array of organocatalysts used in asymmetric reactions (Figure 1).[3] Theoretical and experimental studies

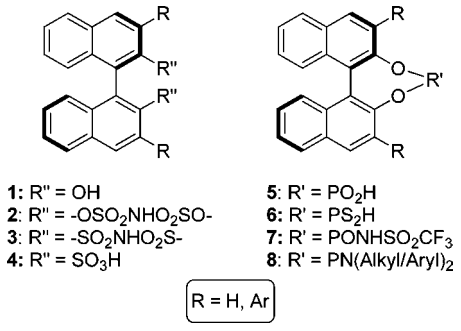


Figure 1. Examples of BINOL derived organocatalysts.

have shown that aryl substitution at the 3 and 3′ positions on the BINOL backbone have considerable influence on these catalysts.[4] Although many of these compounds are commercially available, they are expensive. The high cost is likely due to the tedious chemical manipulations required for the synthesis of these moieties from the corresponding unsubstituted BINOL. Despite a significant growth of interest in these remarkable compounds[3d,4d,5] minimal progress has been made toward efficient preparative methods for enantiomerically pure 3,3′ bis-arylated **1**.[6]

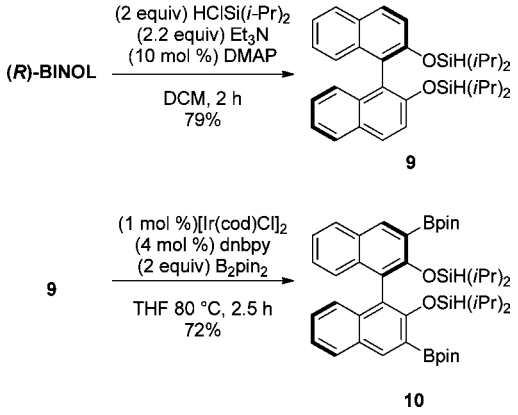
Typically, one of two strategies is employed for the synthesis of 3,3′-bis-arylated **1**. These strategies require the synthesis of either a 3,3′ bis-boronic acid[7] or a 3,3′ bis-halide[8] followed by cross-coupling to install the aryl functional unit. Both approaches require the use of large amounts of alkyllithium reagents as well as the handling of multiple synthetic intermediates and are time-consuming as each intermediate requires purification. They also require protecting group manipulations, which add two additional synthetic operations and purifications.[9] In our hands, the literature sequence[7] required ∼1 week to complete starting from commercially available (*R*)-BINOL. Because asymmetric catalysis demands the rapid screening of catalysts and ligands,[10] we sought a more streamlined approach to 3,3′-bis-arylated BINOL derivatives **1**. We began our investigation by exploring Rh catalyzed C−H arylation[11] of commercially available (*R*)-BINOL as reported by Bedford.[12] C−H arylation products were obtained in moderate yield in refluxing mesitylene after 48 h. Unfortunately, these harsh conditions caused extensive racemization, a known occurrence with BINOL at elevated temperatures.[13] Thus, an alternative approach was sought which would grant access to **1** in good yields while preserving enantiopurity. C−H borylation combined with a subsequent Pd coupling reaction[14] was considered. We were intrigued by Hartwig's protocol for the *ortho*-borylation of phenols.[15] It was envisioned that this could be extended to BINOL, and the resulting boronates could undergo further cross-coupling with an aryl halide.[16] Realization of this hypothesis would grant access to the desired compounds in a single reaction sequence without the need to purify multiple intermediates. Herein we discuss the implementation of this approach for the rapid synthesis of 3,3′ bis-arylated BINOL derivatives.

The synthesis of bis-borylated BINOL intermediate **10** commenced with the formation of diisopropylsilyl ether **9**.[17] Silyl-ether **9** proved to be more stable than the diethyl silyl ethers employed by Hartwig (Scheme 1).[15,18] Diisopropylsilyl ether **9** could be produced as a white crystalline solid in multigram quantities in 79% yield with high enantiopurity.

Received: July 19, 2014
Published: July 31, 2014

   dx.doi.org/10.1021/ol502126r | *Org. Lett.* 2014, 16, 4332−4335

Scheme 1. Silylation and Borylation of (*R*)-BINOL

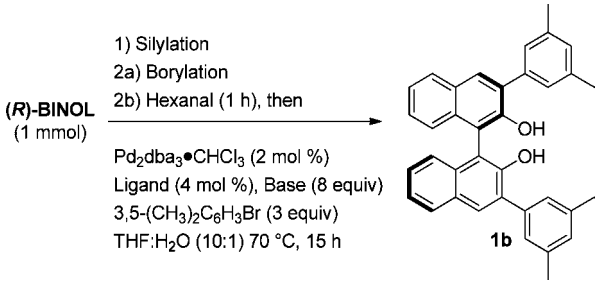


Notably, this material was found to be stable under ambient conditions for several months. Additionally, the protocol developed by Hartwig utilized 4,4′-di-*tert*-butyl-2,2′-bipyridyl (dtbpy) as a ligand. At the time of this work, we found it difficult to obtain dtbpy commercially. Thus, we investigated the related ligand 4,4′-dinonyl-2,2′-bipyridyl (dnbpy), which is also commercially available.[15,19] C−H borylation of **9** afforded bis-borylated intermediate **10** in 72% yield as a white crystalline solid (Scheme 1).

To expedite this sequence, we sought to conduct an *in situ* Suzuki coupling of **10**, ideally in the same reaction flask. It has previously been reported that crude C−H borylation products could be used in Suzuki coupling reactions after removal of all volatile components *in vacuo*, or by filtering the crude reaction mixture through Florisil prior to coupling.[16b,d,20] These precautions were likely implemented to remove boron moieties (i.e., pinacol borane) from the reaction to prevent unwanted side reactions such as reduction of the aryl halide.

Our attempts to use intermediate **10** immediately without isolation or further manipulation provided encouraging results. For example, the reaction mixture was subjected to Suzuki coupling conditions reported by Fu et al.[21] [$Pd(P(t\text{-}Bu)_3)_2$ (1.5 mol %), KF (3.3 equiv), THF, 60 °C, 15 h] to provide trace **1b** (8−10%) in 96% ee (Table 1, entry 1). Despite the low overall yield, it was encouraging that minimal chiral degradation was observed. We reasoned, as aforementioned, the presence of reducing agents derived from pinacol borane and the silyl groups thwarted the Suzuki coupling by reducing the aryl halide. Based on the mechanism proposed by Hartwig,[15] each C−H borylation event affords 1 equiv of pinacol borane. Both borohydrides and silyl hydrides have been reported as hydride sources for reductive coupling reactions using Pd.[22] To perform the desired coupling *in situ*, we posited that the reactive hydrides could be consumed through the use of an additive. To this end, we predicted that the addition of an aldehyde to the reaction vessel could eradicate these reducing agents and improve the overall yield. We anticipated the aldehyde would undergo a hydrosilylation and/or hydroboration event with the corresponding hydrides.[23] We explored the addition of readily available *n*-hexanal and found that adding 2 equiv prior to the *in situ* Suzuki coupling gave 12% of **1b**, while addition of 4 equiv of *n*-hexanal prior to coupling provided 33% of **1b** (Table 1, entries 2 and 3). When 8 equiv of *n*-hexanal were used, a complex mixture was obtained (entry 4). Because there would theoretically be 4 equiv of hydride moieties in the reaction mixture, 4 equiv of the additive were chosen for further study.

Table 1. Addition of Additive and Optimization of Suzuki Conditions



entry	ligand	base (equiv)	*n*-hexanal (equiv)	yield (%)[c]
1	$Pd(P(t\text{-}Bu)_3)_2$[a]	KF[b]	0	8
2	$Pd(P(t\text{-}Bu)_3)_2$[a]	KF[b]	2	12
3	$Pd(P(t\text{-}Bu)_3)_2$[a]	KF[b]	4	33
4	$Pd(P(t\text{-}Bu)_3)_2$[a]	KF[b]	8	ND[d]
5	$P(o\text{-}tolyl)_3$	Na_2CO_3	4	54
6	$P(o\text{-}tolyl)_3$	Cs_2CO_3	4	56
7	$P(o\text{-}tolyl)_3$	K_2CO_3	4	78
8	$P(o\text{-}tolyl)_3$	K_3PO_4	4	76
9	$P(o\text{-}tolyl)_3$	KOAc	4	trace
10	$P(o\text{-}tolyl)_3$	KOH	4	46
11	$P(o\text{-}tolyl)_3$	$Ba(OH)_2$	4	44
12	PPh_3	K_2CO_3	4	53
13	$P(o\text{-}MeOC_6H_4)$	K_2CO_3	4	34
14	$P(p\text{-}MeOC_6H_4)$	K_2CO_3	4	39
15	$HBF_4P(t\text{-}Bu)_3$	K_2CO_3	4	48
16	$HBF_4P(cyclohexyl)_3$	K_2CO_3	4	64

[a]1.5 mol % of $Pd(P(t\text{-}Bu)_3)_2$ was used as the catalyst. [b]3.3 equiv of KF used. [c]Isolated yield **1b**. [d]Yield not determined

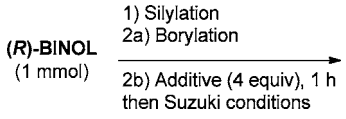
Of note, upon addition of the aldehyde to the reaction mixture an immediate and vigorous gas evolution was observed. This point seems to be in contrast to our hypothesis, and at this juncture, the exact nature of the additive is unknown. However, Hartwig et al. observed a similar phenomenon when $KHF_{2(aq)}$ was added to crude CH-borylation reactions; they presume this was caused by the rapid decomposition of the hydrosilane and pinacol borane to give hydrogen gas.[15]

To optimize the reaction further, Suzuki coupling conditions were explored. Employing a catalyst generated from 2 mol % $Pd_2dba_3{\cdot}CHCl_3$ and 4 mol % $P(o\text{-}tolyl)_3$ with $NaCO_3$ as a base provided **1b** in 54% yield (entry 5).[15] Changing the base to Cs_2CO_3 gave a yield of 56% (entry 6). Since K_2CO_3 provided **1b** in an improved yield of 78% (entry 7), we explored other potassium bases. Use of K_3PO_4 was comparable to K_2CO_3, providing **1b** in 76% yield (entry 8); however, weaker bases such as KOAc gave only trace amounts of **1b** (entry 9). Hydroxide bases, specifically KOH and $Ba(OH)_2$, provided 46% and 44% of **1b**, respectively (entries 10 and 11). Using K_2CO_3 as the base, we examined additional phosphine ligands and observed no improvement in yield (entries 12−16).

With acceptable Suzuki conditions in hand we explored additional aldehydes as additives (Table 2). Isobutyraldehyde, *n*-pentanal, and cyclohexyl carboxaldehyde were comparable to *n*-hexanal and gave yields of 73%, 70%, and 73%, respectively. The bulkier pivaldehyde provided 35% of **1b** (entry 5), and interestingly water could also be used as an additive prior to coupling, albeit with a substantially reduced 28% yield (entry 6). *n*-Hexanal was chosen for our protocol due to cost, availability, and best overall performance.

dx.doi.org/10.1021/ol502126r | *Org. Lett.* 2014, 16, 4332−4335

Table 2. Screen of Additives[a]

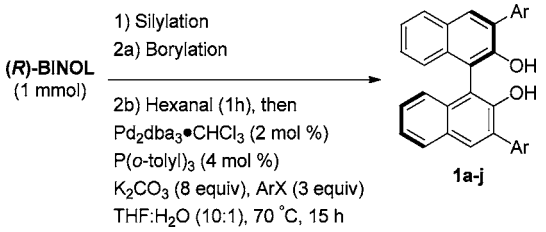


entry	additive (4 equiv)	isolated yield (%)
1	*n*-hexanal	78
2	isobutyraldehyde	73
3	*n*-pentanal	70
4	cyclohexyl carboxyaldehyde	73
5	pivaldehyde	35
6	water	28

[a]Suzuki conditions: $Pd_2dba_3{\cdot}CHCl_3$ (2 mol %), P(*o*-tolyl)$_3$ (4 mol %), K_2CO_3 (8 equiv), 3,5-$(CH_3)_2C_6H_3Br$ (3 equiv), THF/H_2O (10:1), 60 °C, 15 h.

With optimized conditions in hand, we explored the scope of this reaction with regard to the aryl halide coupling partner. Use of iodobenzene, chlorobenzene, and phenyl triflate provided inferior results to bromobenzene (Table 3, entries 1−3). Despite variation in yield, all four reactions provided optically pure **1a**. Utilization of 3,5-dimethyl-bromobenzene and 3,5-bis trifluoromethylbromobenzene afforded **1b** in 78% yield and **1c** in 77% yield, respectively (entries 5 and 6).[24] We were pleased that HPLC analysis of **1b** and **1c** revealed an enantiomeric excess of 96% and 97%, respectively.[25] Electron-poor aryl bromides with *para*-trifluoromethyl, and *para*-nitro groups provided BINOL derivative **1d** in 67% yield, and **1e** in 70% yield, respectively (entries 7−8). Electron-rich 4-bromoanisole afforded **1f** in 63% yield and 87% enantiomeric excess. Bulkier aryl bromides proved more challenging and required the use of SPhos as a ligand.[26] For example, 2-bromo- and 1-bromonaphthalene afforded **1g** in 41% yield and **1h** in 43% yield, respectively, over the three-step sequence (entries 10−11). Similar results were obtained when 9-bromoanthracene derived **1i** was accessed in 53% yield (entry 12). Use of bromomesitylene successfully provided **1j** in 32% yield; however, we were unable to delineate HPLC conditions that provided adequate separation for determination of enantiopurity. Nevertheless, the optical rotation value matched that reported in the literature in both sign and rotation.[27] This three-step reaction sequence also proved to be scalable. As illustrated in Table 3, when this protocol was carried out on a 15 mmol scale, **1a** was obtained in 56% yield (entry 14). As such, 3.75 g of **1a** were acquired in a single run with no loss in enantiopurity.

Table 3. Synthesis of BINOL Derivatives



entry	ArX	isolated yield (%)	$[\alpha]_D^{23}$	% ee[b]
1	PhCl	**1a:** 34	+119.6	>99
2	PhBr	**1a:** 78[a]	+119.6	>99
3	PhI	**1a:** 63	+119.6	>99
4	PhOTf	**1a:** 56	+119.6	>99
5	3,5-$(CH_3)_2C_6H_3Br$	**1b:** 78[a]	+57.2	96
6	3,5-$(CF_3)_2C_6H_3Br$	**1c:** 77[a]	+47.1	97
7	*p*-$CF_3C_6H_4Br$	**1d:** 67	+48.1	93
8	*p*-$NO_2C_6H_4Br$	**1e:** 70	−9.3	94
9	*p*-$MeOC_6H_4Br$	**1f:** 63	+50.1	87
10[c]	2-Br Naphthalene	**1g:** 41	−28.6	91
11[c]	1-Br Naphthalene	**1h:** 43	−12.2	92
12[c,d]	9-Br Anthracene	**1i:** 11	+191.4	93
13[c,d]	Br-Mesitylene	**1j:** 6	+62.1	–[f]
14[e]	PhBr	**1a:** 56	+119.6	>99

[a]Average yield from two runs. [b]Determined by chiral HPLC analysis. [c]S-Phos was used as the ligand in place of P-(*o*-tolyl)$_3$. [d]1,4-Dioxane was used as solvent in place of THF. [e]Reaction performed on 15 mmol scale to yield 3.75 g of **1a**. [f]% ee could not be obtained by chiral HPLC

In summary, we have developed a rapid and scalable process for the preparation of valuable and highly versatile 3,3′ bis-arylated BINOL derivatives. This was accomplished through a three-step protocol consisting of (1) silyl ether formation, (2) CH-borylation, and (3) Suzuki−Miyaura coupling. This process requires only a single chromatography step, and the entire sequence can be completed within 24 h. The utilization of *n*-hexanal as an additive facilitated a successful one-pot C−H-borylation/Suzuki coupling. This method was particularly well suited for substituted aryl bromides and furnishes the desired BINOL derivatives in excellent yield and high enantiopurity.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, characterization data, and additional results. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: daclar01@syr.edu.

Present Address

[†]Department of Chemistry, Syracuse University, 1-014 Center for Science and Technology, Syracuse, New York 13244-4100.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Syracuse University for the generous financial support of this research. We thank the Chisholm and Totah research groups (Syracuse University) for sharing of reagents, instrumentation, and helpful discussions.

■ REFERENCES

(1) (a) Rousseaux, S.; Liégault, B.; Fagnou, K. *Modern Tools for the Synthesis of Complex Bioactive Molecules*; John Wiley & Sons, Inc.: 2012; pp 1−32. (b) MacCoss, M.; Baillie, T. A. *Science* **2004**, *303*, 1810.

(2) (a) Le, P. Q.; Nguyen, T. S.; May, J. A. *Org. Lett.* **2012**, *14*, 6104. (b) Luan, Y.; Schaus, S. E. *J. Am. Chem. Soc.* **2012**, *134*, 19965. (c) Zhang, Y.; Li, N.; Qu, B.; Ma, S.; Lee, H.; Gonnella, N. C.; Gao, J.; Li, W.; Tan, Z.; Reeves, J. T.; Wang, J.; Lorenz, J. C.; Li, G.; Reeves, D. C.; Premasiri, A.; Grinberg, N.; Haddad, N.; Lu, B. Z.; Song, J. J.; Senanayake, C. H. *Org. Lett.* **2013**, *15*, 1710. (d) Vallakati, R.; Lundy, B. J.; Jansone-Popova, S.; May, J. A. Biomimetic Synthesis and Studies Toward Enantioselective Synthesis of Flindersial Alkaloids. *Chirality*

2013, [Online early access] DOI:10.1002/chir.22134. (e) Saito, K.; Shibata, Y.; Yamanaka, M.; Akiyama, T. *J. Am. Chem. Soc.* **2013**, *135*, 11740. (f) Maity, P.; Pemberton, R. P.; Tantillo, D. J.; Tambar, U. K. *J. Am. Chem. Soc.* **2013**, *135*, 16380.

(3) (a) Nakashima, D.; Yamamoto, H. *J. Am. Chem. Soc.* **2006**, *128*, 9626. (b) Shapiro, N. D.; Rauniyar, V.; Hamilton, G. L.; Wu, J.; Toste, F. D. *Nature* **2011**, *470*, 245. (c) Cheon, C. H.; Yamamoto, H. *Chem. Commun.* **2011**, *47*, 3043. (d) List, B.; Reisinger, C. M.; Kampen, D. *Chiral Bronsted Acids for Asymmetric Organocatalysis*; SpringerLink: 2009; Vol. *291*. (e) Terada, M. *Chem. Commun.* **2008**, 4097. (f) Zamfir, A.; Schenker, S.; Freund, M.; Tsogoeva, S. B. *Org. Biomol. Chem.* **2010**, *8*, 5262. (g) Singh, R.; Czekelius, C.; Schrock, R. R.; Müller, P.; Hoveyda, A. H. *Organometallics* **2007**, *26*, 2528. (h) Rowland, G. B.; Zhang, H.; Rowland, E. B.; Chennamadhavuni, S.; Wang, Y.; Antilla, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 15696. (i) Pousse, G.; Devineau, A.; Dalla, V.; Humphreys, L.; Lasne, M.-C.; Rouden, J.; Blanchet, J. *Tetrahedron* **2009**, *65*, 10617. (j) Teichert, J. F.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2010**, *49*, 2486. (k) Berkessel, A.; Christ, P.; Leconte, N.; Neudörfl, J.-M.; Schäfer, M. *Eur. J. Org. Chem.* **2010**, *2010*, 5165. (l) Treskow, M.; Neudörfl, J.; Giernoth, R. *Eur. J. Org. Chem.* **2009**, *2009*, 3693. (m) García-García, P.; Lay, F.; García-García, P.; Rabalakos, C.; List, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 4363. (n) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1566. (o) Uraguchi, D.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 5356. (p) Eggenstein, M.; Thomas, A.; Theuerkauf, J.; Franciò, G.; Leitner, W. *Adv. Synth. Catal.* **2009**, *351*, 725.

(4) (a) Kaupmees, K.; Tolstoluzhsky, N.; Raja, S.; Rueping, M.; Leito, I. *Angew. Chem., Int. Ed.* **2013**, *52*, 11569. (b) Yang, C.; Xue, X.-S.; Jin, J.-L.; Li, X.; Cheng, J.-P. *J. Org. Chem.* **2013**, *78*, 7076. (c) Brunel, J. M. *Chem. Rev.* **2005**, *105*, 857. (d) Terada, M. *Chem. Soc. Jpn.* **2010**, *83*, 101. (e) Chen, Y.; Yekta, S.; Yudin, A. K. *Chem. Rev.* **2003**, *103*, 3155.

(5) (a) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744. (b) Rueping, M.; Nachtsheim, B. J.; Ieawsuwan, W.; Atodiresei, I. *Angew. Chem., Int. Ed.* **2011**, *50*, 6706.

(6) (a) Lee, C.-Y.; Cheon, C.-H. *J. Org. Chem.* **2013**, *78*, 7086. (b) Truong, T.; Daugulis, O. *Chem. Sci.* **2013**, *4*, 531. (c) Li, B.; Chiu, P. *Eur. J. Org. Chem.* **2011**, *2011*, 3932.

(7) Wipf, P.; Jung, J.-K. *J. Org. Chem.* **2000**, *65*, 6319.

(8) (a) Wu, T. R.; Shen, L.; Chong, J. M. *Org. Lett.* **2004**, *6*, 2701. (b) Rueping, M.; Nachtsheim, B. J.; Koenigs, R. M.; Ieawsuwan, W. *Chem.—Eur. J.* **2010**, *16*, 13116. (c) Cox, P. J.; Wang, W.; Snieckus, V. *Tetrahedron Lett.* **1992**, *33*, 2253.

(9) (a) Young, I. S.; Baran, P. S. *Nat. Chem.* **2009**, *1*, 193. (b) Newhouse, T.; Baran, P. S.; Hoffmann, R. W. *Chem. Soc. Rev.* **2009**, *38*, 3010.

(10) (a) de Vries, J. G.; Lefort, L. *Chem.—Eur. J.* **2006**, *12*, 4722. (b) Blaser, H. U.; Spindler, F.; Studer, M. *Appl. Catal. A: General* **2001**, *221*, 119. (c) Hawkins, J. M.; Watson, T. J. N. *Angew. Chem., Int. Ed.* **2004**, *43*, 3224.

(11) (a) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (b) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (c) Kakiuchi, F.; Kochi, T. *Synthesis* **2008**, 3013. (d) Li, B.-J.; Yang, S.-D.; Shi, Z.-J. *Synlett* **2008**, 949. (e) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (f) Rostovtsev, V. V. In *Handbook of C—H Transformations*; Wiley-VCH Verlag GmbH: 2008; p 99. (g) Truong, T.; Daugulis, O. *Angew. Chem., Int. Ed.* **2012**, *51*, 11677.

(12) Bedford, R. B.; Betham, M.; Caffyn, A. J. M.; Charmant, J. P. H.; Lewis-Alleyne, L. C.; Long, P. D.; Polo-Ceron, D.; Prashar, S. *Chem. Commun.* **2008**, 990.

(13) (a) Noji, M.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1994**, *35*, 7983. (b) Kyba, E. P.; Gokel, G. W.; De Jong, F.; Koga, K.; Sousa, L. R.; Siegel, M. G.; Kaplan, L.; Sogah, G. D. Y.; Cram, D. J. *J. Org. Chem.* **1977**, *42*, 4173.

(14) (a) Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E., Jr.; Smith, M. R., III. *Science* **2002**, *295*, 305. (b) Kallepalli, V. A.; Sanchez, L.; Li, H.; Gesmundo, N. J.; Turton, C. L.; Maleczka, R. E., Jr.; Smith, M. R., III. *Heterocycles* **2010**, *80*, 1429. (c) Norberg, A. M.; Smith, M. R., III; Maleczka, R. E., Jr. *Synthesis* **2011**, *2011*, 857.

(15) Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 7534.

(16) (a) Cho, S. H.; Hartwig, J. F. *Chem. Sci.* **2014**, *5*, 694. (b) Partridge, B. M.; Hartwig, J. F. *Org. Lett.* **2012**, *15*, 140. (c) Ros, A.; López-Rodríguez, R.; Estepa, B.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 4573. (d) Robbins, D. W.; Hartwig, J. F. *Org. Lett.* **2012**, *14*, 4266.

(17) Huang, C.; Gevorgyan, V. *Org. Lett.* **2010**, *12*, 2442.

(18) Murphy, P. D.; Taki, T.; Sogabe, T.; Metzler, R.; Squires, T. G.; Gerstein, B. C. *J. Am. Chem. Soc.* **1979**, *101*, 4055.

(19) (a) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2009**, *110*, 890. (b) We later obtained dtbpy and utilized it in the reaction to provide **1b** in 74% yield. For a new synthetic method toward dtbpy, see: Buonomo, J. A.; Everson, D. A.; Weix, D. J. *Synthesis* **2013**, *45* (15), 3099.

(20) (a) Tobisu, M.; Fujihara, H.; Koh, K.; Chatani, N. *J. Org. Chem.* **2010**, *75*, 4841. (b) Chotana, G. A.; Kallepalli, V. A.; Maleczka, R. E., Jr.; Smith, M. R., III. *Tetrahedron* **2008**, *64*, 6103.

(21) Fu, G. C. *Acc. Chem. Res.* **2008**, *41*, 1555.

(22) (a) Yang, J.; Brookhart, M. *J. Am. Chem. Soc.* **2007**, *129*, 12656. (b) Yamanoi, Y. *J. Org. Chem.* **2005**, *70*, 9607. (c) Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **1999**, *65*, 164.

(23) (a) Park, S.; Brookhart, M. *Organometallics* **2010**, *29*, 6057. (b) Arrowsmith, M.; Hadlington, T. J.; Hill, M. S.; Kociok-Kohn, G. *Chem. Commun.* **2012**, *48*, 4567. (c) Wile, B. M.; Stradiotto, M. *Chem. Commun.* **2006**, 4104. (d) Shaikh, N. S.; Junge, K.; Beller, M. *Org. Lett.* **2007**, *9*, 5429.

(24) Isolated bis-silyl ether **9** could be subjected to the aforementioned C—H borylation/Suzuki coupling protocol. For example, 1 mmol of bis-silyl ether **9** was converted to **1b** with a 73% yield.

(25) Akiyama, T.; Morita, H.; Itoh, J.; Fuchibe, K. *Org. Lett.* **2005**, *7*, 2583.

(26) (a) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685. (b) Billingsley, K.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3358.

(27) Yamanaka, M.; Itoh, J.; Fuchibe, K.; Akiyama, T. *J. Am. Chem. Soc.* **2007**, *129*, 6756.