Communication

Double N,B-type Bidentate Boryl Ligands Enabling a Highly Active Iridium Catalyst for C-H Borylation

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Double N,B-type Bidentate Boryl Ligands Enabling a Highly Active Iridium Catalyst for C-H Borylation

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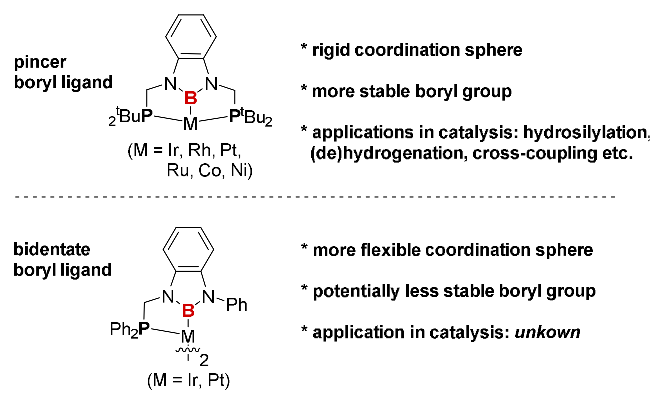
Supporting Information Placeholder

ABSTRACT: Boryl ligands hold promise in catalysis due to their very high electron-donating property. In this communication double N,B-type boryl anions were designed as bidentate ligands to promote sp^2 C-H borylation reaction. A symmetric pyridine-containing tetraaminodiborane(4) compound (**1**) was readily prepared as the ligand precursor that could be used, in combination with $[Ir(OMe)(COD)]_2$, to *in situ* generate a highly active catalyst for a broad range of (hetero)arene substrates including highly electron-rich and/or sterically hindered ones. This work provides the first example of a bidentate boryl ligand in supporting homogeneous organometallic catalysis.

Transition metal boryl complexes have been proposed or identified as the key active intermediates in many types of stoichiometric and catalytic organometallic reactions.[1] Because of its vacant p_z orbital and extremely σ-electron-releasing property,[2] the sp^2 boryl anion usually behaves as a "reactive" ligand, i.e., to be transferred from the metal centers to the final product.[1] In order to further exploit the unique property of boryl ligands, in 2009, Yamashita and Nozaki, and Mirkin independently reported their works on XBX (X = P, Se, S) pincer-type tridentate "supporting" ligands and related transition metal complexes.[3] Since then the chemistry of pincer boryl ligands and their transition metal complexes have rapidly advanced in recent years[4] (Figure 1) and their applications in homogeneous catalysis including hydrosilylation, (de)hydrogenation and cross-coupling reactions have appeared.[5] In contrast, although bidentate ligands may provide more flexible coordination spheres and some related transition metal boryl complexes have been described,[6] to the best of our knowledge, no catalytic reactions involving a supporting bidentate boryl ligand have been reported before. Herein, we present our results in developing a convenient ligand precursor for introducing NB-type bidentate ligands and its application in a highly active iridium-catalyzed C-H borylation reaction.

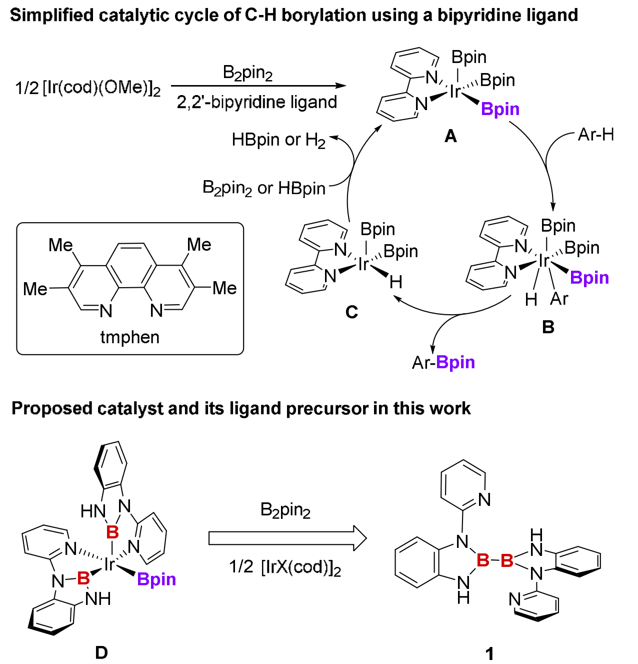
Transition metal-catalyzed arene C-H borylation is a powerful and atom-economic method for C-B bond formation[7,8] and the resulting arylboron compounds are widely useful building blocks in organic synthesis, drug discovery and materials science.[9] Among the known catalyst systems for this transformation, iridium catalysts supported by 2,2'-bipyridine type ligands[7f] have found the broadest applications, and within them, recent comprehensive studies have revealed that 3,4,7,8-tetramethyl-1,10-phenanthroline (tmphen) usually leads to the most active catalyst.[10] Mechanistically, a bipyridine-coordinated Ir(III) trisboryl complex (**A**, in Scheme 1) is believed to be the real catalyst. **A** undergoes oxidative addition with an arene C-H bond to form Ir(V) complex **B**, which produces the aryl boronate by C-B reductive elimination and Ir(III) hydride **C**. Catalyst **A** can be regenerated via hydride-boryl metathesis from **C**. Previous experimental and computational studies have pointed out that the oxidative addition of C_{Ar}-H to **A** is often the rate-determining step.[11] Consequently, it is conceivable that more electron-donating ligands might promote faster oxidative addition and hence higher catalytic activity. Since only one of the three boryl ligands (in purple) is actually needed for the product formation in one catalytic cycle, we wondered whether the rest two boryl ligands could be selectively preinstalled and modified as supporting ligands, thus providing new opportunities in tuning the electronic and steric proper-

Figure 1. Pincer-type Tridentate and Bidentate Boryl Ligands: Representative Structures, Properties and Applications



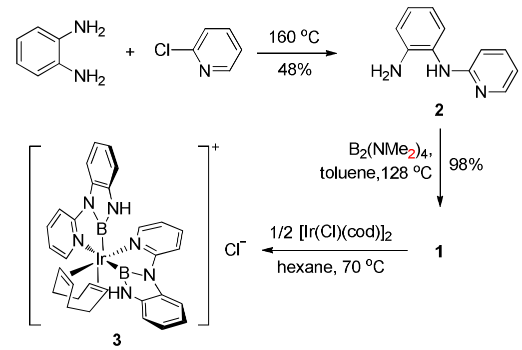
ties of the catalyst center. Therefore, we proposed structure **D** as a potential catalyst (Scheme 1) by recombining the bipyridine ligand and two boryls into two N,B-type bidentate ligands.[12] We substituted the 1,3,2-dioxaborole of Bpin by a 1,3,2-diazaborole unit in the hope of enhancing the electron-donating propensity of both the boryl and pyridine ligands. Iridium complex **D** might be formed from B-B oxidative addition of a ligand precursor **1** to iridium precatalyst followed by metathetic reaction with the borylation reagent.

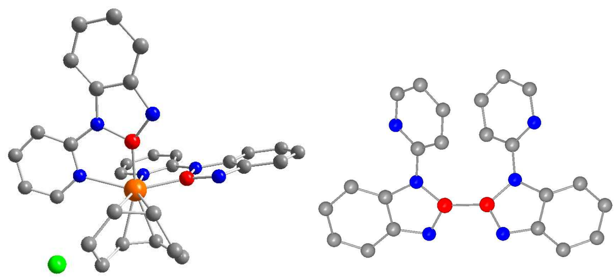
Scheme 1. Rational Design of Preligand 1



The synthetic route to preligand **1** is shown in Scheme 2. Simply heating a neat mixture of *o*-phenylenediamine with 1.1 equiv of 2-chloropyridine gave N-(2-pyridyl)-phenylenediamine **2** in 48% isolated yield. Treatment of **2** with 0.6 equiv of 1,1,2,2-tetrakis(dimethylamino)-diborane(4) (^{11}B NMR: 36.8 ppm) at 128 °C in toluene cleanly gave a new compound (^{11}B NMR: 28.7 ppm) in excellent yield. The structure of this product was determined by single crystal X-ray crystallography to be the desired tetraaminodiborane(4) **1** (Figure 2).[13] When a solution of **1** and 0.5 equiv of [Ir(Cl)(cod)]$_2$ in hexane was heated at 70 °C for 10 hours, a complex (**3**) was formed in 83% NMR spectroscopic yield. A single crystal of **3** suitable for X-ray analysis was obtained from CH_2Cl_2/hexane solution and the molecular structure is shown in Figure 2. This ionic iridium complex adopts a distorted octahedral configuration containing two N,B-bidentate boryl ligands and a cod ligand. An unusual outersphere chloride anion is formed in the absence of any sequesters. Interestingly, the two pyridine and the two boryl ligands all take a *cis* relationship resembling the 2,2'-bipyridine-based catalyst **A** and our proposed catalyst **D** (Scheme 1). Therefore, via B-B oxidative addition of **1**, iridium complexes with an [NB-Ir^{III}-BN] framework can be readily accessed, paving the way for the catalyst generation.

Scheme 2. Preparation of Preligand 1 and Its Oxidative Addition with [Ir(Cl)(cod)]$_2$.





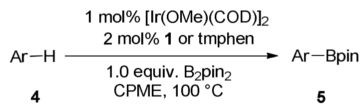
3 1

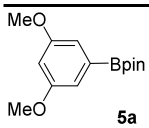
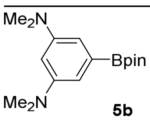
Figure 2. Molecular structures of preligand **1** and complex **3** (50% thermal ellipsoids; hydrogen atoms in **3** were omitted for clarity). Ir: orange; B: red; N: blue; C: gray; Cl: green.

To test the effectiveness of preligand **1** in iridium-catalyzed C-H borylation, 1,3-dimethoxybenzene (**4a**) was chosen as a challenging benchmark substrate due to its high electron richness.[10a] After some optimizations (see Supporting Information), pleasingly, **1** was found indeed very effective in promoting the desired borylation. Thus, a mixture of the precatalyst [Ir(OMe)(COD)]$_2$ (1 mol%), the preligand **1** (2 mol%), B$_2$pin$_2$ (1.0 equiv.) and **4a** was heated at 100 °C in cyclopentyl methyl ether (CPME) for 16 hours, leading to nearly quantitative formation of the desired product **5a** (98% NMR and 95% isolated yield, Table 1). In comparison, when tmphen was used as the supporting ligand under otherwise identical conditions, significantly lower yield of **5a** (81% ^{1}H NMR and 78% isolated) was formed together with some unidentifiable side products. To further test the efficiency of preligand **1** on a more electron-rich substrate, the borylation of N^1,N^1,N^3,N^3-tetramethylbenzene-1,3-diamine was conducted. Again, clean conversion to the aryl boronate **5b** was observed (94% NMR and 93% isolated yield) in 24 hours, while only 50% conversion was reached using tmphen as the ligand.

Encouraged by the preliminary results, we explored the substrate scope of preligand **1**-based catalytic boryation (Table2). Under the above established conditions, both electron-rich and electron-poor arenes, containing alkoxy, dialkylamino, halogen, ester groups, were all transformed to the aryl boronates in excellent yields (**5c**-**5p**). Acetyl and cyano groups seemed to slow down the reaction. At higher temperatures, however, useful yields of the meta-borylation products could be isolated (**5q**, **5r**). The borylation of ferrocene with 1.0 equivalent of B$_2$pin$_2$ produced a mixture of mono-, 1,1'-di-, 1,3-di- and 1,3,1'-triborylated products (67:9:14:10) and the mono-borylation product **5s** could be isolated in good yield. Heteroarenes including thiophene (**5t**, **5u**), benzofuran (**5v**), pyridines (**5w**, **5x**) and indoles (**5y**, **5z**) were also good substrates, affording synthetically important organoboron reagents in a step-economic fashion. Among them, differentiated diborylated compound **5u** is a versatile intermediate for modular synthesis of functionalized thiophene derivatives.[14] The regioselective 7-borylation of 2-methylindole (**5y**) was probably via a directed C-H activation mechanism similar to the previous report based on 2,2'-bipyridine ligands.[15]

Table 1. Comparison of Preligand 1 with Tmphen in Borylation of Electron-rich Substrates[a]



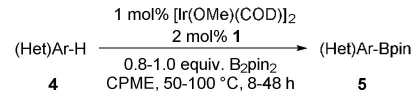
Product	Preligand 1		tmphen	
	Conv. (%)[b]	Yield (%)[b,c]	Conv. (%)[b]	Yield (%)[b,c]
 **5a**	98	98 (95)	94	81 (78)
 **5b**	94	94 (93)	50	50 (49)

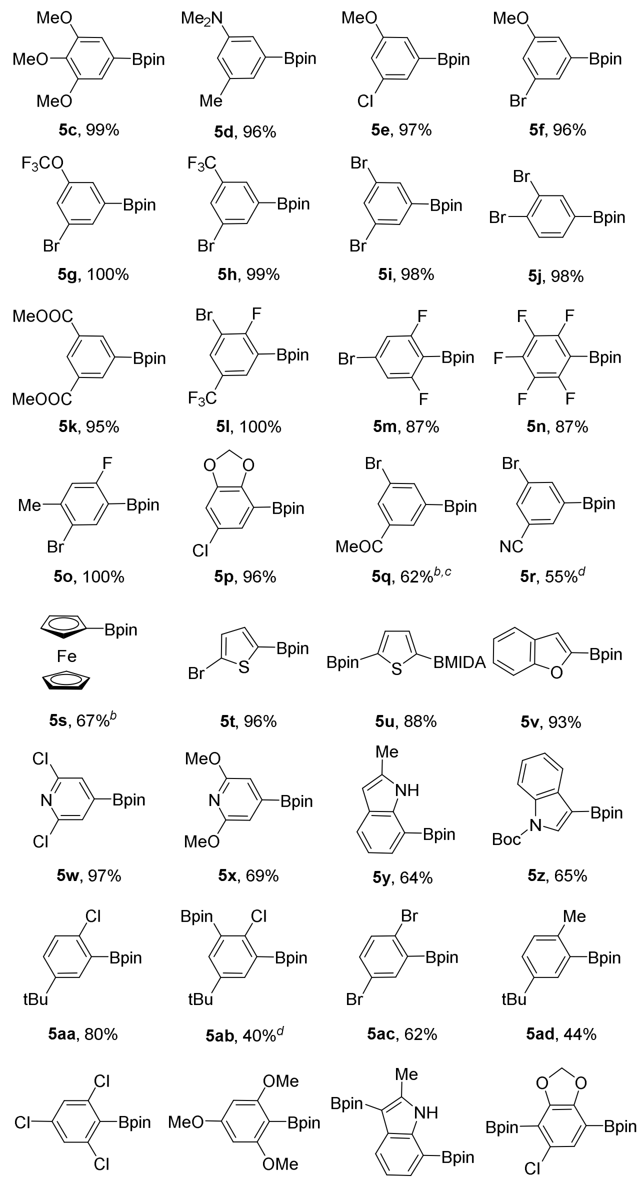
[a]Reaction conditions: arene **4** (0.5 mmol), B_2pin_2 (0.5 mmol), $[Ir(OMe)(COD)]_2$ (0.005 mmol), **1** or tmphen (0.01 mmol) in 1.0 mL CPME, 100 °C. [b]Coversions and yields were based on ^1H NMR analyses of the crude products with 1,3,5-trimethoxybenzene as an internal standard. [c]isolated yields in parentheses. tmphen: 3,4,7,8-tetramethyl-1,10-phenanthroline; CPME: cyclopentyl methyl ether.

Because the Ir-catalyzed borylation is usually very sensitive to steric hindrance, we questioned if the current catalyst system is effective for sterically encumbered substrates. As shown in Table2, monoborylation at the *ortho* position to a chlorine, bromine and methyl groups were all feasible, leading to the corresponding products in good to moderate yields, roughly reflecting the bulkiness of the relevant substituents (**5aa**-**5ad**). The reaction using excess of B_2pin_2 and at higher temperature (150 °C) gave 2,6-diborylation product **5ab**. 1,3,5-Trichlorobenzene, a sterically more hindered substrate was also viable and the product could be isolated in useful yield (**5ae**, 49%). The more electron-rich and more bulky compound 1,3,5-trimethoxybenzene was only borylated in low yield (**5af**, 20%). Finally, 2-methylindole and 5-chloro-1,3-benzodioxole could be selectively transformed to their mono- or diborylation products in good yields depending on the reaction conditions (**5ag** vs. **5y**, **5ah** vs. **5p**, for reaction details see SI).

In summary, we have designed and prepared a symmetric dipyridinyl tetraaminodiborane(4) (**1**) and proved its usefulness as a precursor for introducing double N,B-type boryl ligands onto iridium via B-B oxidative addition. Based on this preligand, we have developed a highly active iridium catalyst system for C-H borylation of various (hetero)arenes, including highly electron-rich ones and sterically hindered ones. This work has successfully employed bidentate boryl anion(s) as supporting ligand(s) in transition metal catalysis for the first time and may inspire the discovery of interesting transition metal complexes and new catalytic systems based on similar ligand frameworks.

Table 2. Substrate Scope of C-H Borylation using Preligand 1[a]





5c, 99%; **5d**, 96%; **5e**, 97%; **5f**, 96%; **5g**, 100%; **5h**, 99%; **5i**, 98%; **5j**, 98%; **5k**, 95%; **5l**, 100%; **5m**, 87%; **5n**, 87%; **5o**, 100%; **5p**, 96%; **5q**, 62%[b,c]; **5r**, 55%[d]; **5s**, 67%[b]; **5t**, 96%; **5u**, 88%; **5v**, 93%; **5w**, 97%; **5x**, 69%; **5y**, 64%; **5z**, 65%; **5aa**, 80%; **5ab**, 40%[d]; **5ac**, 62%; **5ad**, 44%; **5ae**, 49%; **5af**, 20%[d]; **5ag**, 77 %; **5ah**, 65%

[a]See SI for experimental details. Yields are all for isolated yields. [b]Reaction temperature 125 °C. [c]0.75 mmol of B_2pin_2. [d]Reaction temperature 150 °C.

ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures, spectral data of products and X-ray crystallographic data for **1** and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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REFERENCES

(1) (a) Irvine, G. J.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R.; Robins, E. G.; Roper, W. R.; Whittell, G. R.; Wright, L. J. *Chem. Rev*. **1998**, *98*, 2685. (b) Aldridge, S.; Coombs, D. L. *Coord. Chem. Rev*. **2004**, *248*, 535. (c) Dang, L.; Lin, Z.; Marder, T. B. *Chem. Commun.* **2009**, 3987. (d) Braunschweig, H.; Dewhurst, R. D.; Schneider, A. *Chem. Rev*. **2010**, *110*, 3924.

(2) (a) Dettenrieder, N.; Aramaki, Y.; Wolf, B. M. Maichle-Mössmer, C.; Zhao, X.; Yamashita, M.; Nozaki, K.; Anwander, R. *Angew. Chem. Int. Ed.* **2014**, *53*, 6259. (b) Segawa, Y.; Yamashita, M.; Nozaki, K. *Science* **2006**, *314*, 113. (c) Segawa, Y.; Suzuki, Y.; Yamashita, M.; Nozaki, K. *J. Am. Chem. Soc.* **2008**, *130*, 16069. (d) Zhu, J.; Lin, Z.; Marder, T. B. *Inorg. Chem.* **2005**, *44*, 9384. (e) Braunschweig, H.; Brenner, P.; Müller, A.; Radacki, K.; Rais, D.; Uttinger, K. *Chem. - Eur. J.* **2007**, *13*, 7171. (f) Braunschweig, H.; Radacki, K.; Uttinger, K. *Chem. - Eur. J.* **2008**, *14*, 7858.

(3) (a) Segawa, Y.; Yamashita, M.; Nozaki, K. *J. Am. Chem. Soc.* **2009**, *131*, 9201. (b) Spokoyny, A. M.; Reuter, M. G.; Stern, C. L.; Ratner, M. A.; Seideman, T.; Mirkin, C. A. *J. Am. Chem. Soc.* **2009**, *131*, 9482.

(4) (a) For a highlight, see: van der Vlugt, J. I. *Angew. Chem. Int. Ed.* **2009**, *49*, 252. (b) Hill, A. F.; Lee, S. B.; Park, J.; Shang, R.; Willis, A. C. *Organometallics* **2010**, *29*, 5661. (c) El-Zaria, M. E.; Arii, H.; Nakamura, H. *Inorg. Chem.* **2011**, 50, 4149. (d) Hasegawa, M.; Segawa, Y.; Yamashita, M.; Nozaki, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 6956. (e) Miyada, T.; Yamashita, M. *Organometallics* **2013**, *32*, 5281. (f) Hill, A. F.; McQueen, C. M. A. *Organometallics* **2014**, *33*, 1977. (g) Curado, N.; Maya, C.; Lopez-Serrano, J.; Rodriguez, A. *Chem. Commun.* **2014**, *50*, 15718.

(5) (a) Ogawa, H.; Yamashita, M. *Dalton Trans*. **2013**, *42*, 625. (b) Lin, T.-P.; Peters, J. C. *J. Am. Chem. Soc.* **2013**, *135*, 15310. (c) Masuda, Y.; Hasegawa, M.; Yamashita, M.; Nozaki, K.; Ishida, N.; Murakami, M. *J. Am. Chem. Soc.* **2013**, *135*, 7142. (d) Lin, T.-P.; Peters, J. C. *J. Am. Chem. Soc.* **2014**, *136*, 13672. (e) Tsang, M. Y.; Viñas, C.; Teixidor, F.; Planas, J. G.; Conde, N.; SanMartin, R.; Herrero, M. T.; Domínguez, E.; Lledós, A.; Vidossich, P.; Choquesillo-Lazarte, D. *Inorg. Chem.* **2014**, *53*, 9284.

(6) (a) Lu, Z.; Jun, C.-H.; de Gala, S. R.; Sigalas, M. P.; Eisenstein, O.; Crabtree, R. H. *Organometallics* **1995**, *14*, 1168. (b) Irvine, G. J.; Rickard, C. E. F.; Roper, W. R.; Williamson, A.; Wright, L. J. *Angew. Chem. Int. Ed.* **2000**, *39*, 948. (c) Rickard, C. E. F.; Roper, W. R.; Williamson, A.; Wright, L. J. *Organometallics* **2002**, *21*, 1714. (d) Rickard, C. E. F.; Roper, W. R.; Williamson, A.; Wright, L. J. *Organometallics* **2002**, *21*, 4862. (e) Braunschweig, H.; Lutz, M.; Radacki, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 5647. (f) Braunschweig, H.; Kupfer, T.; Lutz, M.; Radacki, K.; Seeler, F.; Sigritz, R. *Angew. Chem. Int. Ed.* **2006**, *45*, 8048. (g) Schubert, H.; Leis, W.; Mayer, H. A.; Wesemann, L. *Chem. Commun.* **2014**, 50, 2738.

(7) For leading reviews, see: (a) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890. (b) J. F. Hartwig, *Acc. Chem. Res.* **2012**, *45*, 864; c) Ros, A.; Fernandez, R.; Lassaletta, J. M. *Chem. Soc. Rev.* **2014**, *43*, 3229. (d) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2003**, *680*, 3. (e) Hartwig, J. F. *Chem. Soc. Rev.* **2011**, *40*, 1992. (f) Ishiyama, T.; Miyaura, N. *Pure Appl. Chem.* **2006**, *78*, 1369.

(8) For selected references of arene C-H borylation, see: (a) Iverson, C. N.; Smith, III M. R. *J. Am. Chem. Soc.* **1999**, *121*, 7696. (b) Chen, H.; Schlecht, S.; Semple, T. C.; Hartwig, J. F. *Science* **2000**, *287*, 1995. (c) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390. (d) Kawamorita, S.; Ohmiya, H.; Hara, K.; Fukuoka, A.; Sawamura, M. *J. Am. Chem. Soc.* **2009**, *131*, 5058. (e) Mkhalid, I. A. I.; Coventry, D. N.; Jove, D. A.; Batsanov, A. S.; Howard, J. A. K.; Perutz, R. N.; Marder, T. B. *Angew. Chem. Int. Ed.* **2006**, *45*, 489. (f) Ros, A.; Estepa, B.; López-Rodriguez, R.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *Angew. Chem. Int. Ed.* **2011**, *50*, 11724. (g) Dai, H. X.; Yu, J. Q. *J. Am. Chem. Soc.* **2012**, *134*, 134. (h) Kawamorita, S.; Murakami, R.; Iwai, T.; Sawamura, M. *J. Am. Chem. Soc.* **2013**, *135*, 2947 (i) Mazzacano, T. J.; Mankad, N. P. *J. Am. Chem. Soc.* **2013**, *135*, 17258. (j) Obligacion, J. V.; Semproni, S. P.; Chirik, P. J. *J. Am. Chem. Soc.* **2014**, *136*, 4133. (k) Dombray, T.; Werncke, C. G.; Jiang, S.; Grellier, M.; Vendier, L.; Bontemps, S.; Sortais, J.-B.; Sabo-Etienne, S.; Darcel, C. *J. Am. Chem. Soc.* **2015**, *137*, 4062.

(9) *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials*; Hall, D., Ed.; Wiley-VCH, Weinheim, Germany, 2011.

(10) (a) Preshlock, S. M.; Ghaffari, B.; Maligres, P. E.; Krska, S. W.; Maleczka, R. E.; Smith, M. R. *J. Am. Chem. Soc.* **2013**, *135*, 7572. (b) Larsen, M. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 4287.

(11) (a) Boller, T. M.; Murphy, J. M.; Hapke, M.; Ishiyama, T.; Miyaura, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 14263. (b) Tamura, H.; Yamazaki, H.; Sato, H.; Sakaki, S. *J. Am. Chem. Soc.* **2003**, *125*, 16114. (c) Vanchura, B. A.; Preshlock, S. M.; Roosen, P. C.; Kallepalli, V. A.; Staples, R. J.; Maleczka, R. E.; Singleton, D. A.; Smith, M. R. *Chem. Commun.* **2010**, *46*, 7724. (d) Green, A. G.; Liu, P.; Merlic, C. A.; Houk, K. N. *J. Am. Chem. Soc.* **2014**, *136*, 4575.

(12) For bidentate and tridentate silyl ligands in C-H borylation, see: (a) Ghaffari, B.; Preshlock, S. M.; Plattner, D. L.; Staples, R. J.; Maligres, P. E.; Krska, S. W.; Maleczka, Jr., R. E.; Smith, III M. R. *J. Am. Chem. Soc.* **2014**, *136*, 14345. (b) Lee, C.-I.; Zhou, J.; Ozerov, O. V. *J. Am. Chem. Soc.* **2013**, *135*, 3560.

(13) For leading references of tetraaminodiborane(4) compounds, see: (a) Loderer, D.; Noth, H.; Pommerening H.; Rattay, W.; Schick, H. *Chem. Ber.* **1994**, *127*, 1605. (b) Alibadi, M. A.; Batsanov, A. S.; Bramham, G.; Charmant, J. P.; Haddow, M. F.; Mackay, L.; Mansell, S. M.; McGrady, J. E.; Norman, N. C.; Roffey, A.; Russell, C. A. *Dalton Trans*. **2009**, 5348. (c) Xie, X.; Haddow, M. F.; Mansell, S. M.; Norman, N. C.; Russell, C. A. *Dalton Trans*. **2012**, *41*, 5348.

(14) (a) Xu, L.; Ding, S.; Li, P. *Angew. Chem. Int. Ed.* **2014**, *53*, 1822. (b) Xu, L.; Li, P. *Synlett* **2014**, *25*, 1799. (c) Xu, L.; Li, P. *Chem. Commun.* **2015**, *51*, 5656.

(15) Paul, S.; Chotana, G. A.; Holmes, D.; Reichle, R. C.; Maleczka, R. E.; Smith, M. R. *J. Am. Chem. Soc.* **2006**, *128*, 15552.

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