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Doctoral Dissertation

Studies on Catalytic Borylation and Reduction Reactions Using Aminoborane Reagents

Takuya Igarashi

January 2019

Department of Applied Chemistry,
Graduate School of Engineering,
Osaka University

Preface and Acknowledgement

The research presented in this thesis was carried out under the direction of Professor Naoto Chatani and Professor Mamoru Tobisu of the Department of Applied Chemistry, Faculty of Engineering, Osaka Unversity from April 2014 to March 2019. The thesis is concerned with catalytic borylation and reduction reactions using aminoborane reagents.

This thesis could not have been completed without the support from numerous people. Here, I wish to express my sincerest appreciation to all of those people.

First of all, I express utmost appreciation to Professor Naoto Chatani. He showed me the way to live as a reasearcher in my laboratory life. I learned from him that, in order to survive as a researcher, it is essential to think thoroughly about chemistry, and to be a hard worker. Above all, his words remained in my heart strongly that the desire to get promoted is important. I would like continue striving to be a respectable researcher like him.

I would also like to express my deepest gratitude to Professor Mamoru Tobisu for his valuable and continuous support. It is thanks to his excellent surpoort that I submitted papers at an early stage, despite being later to start my original research than other students. His creative and logical advice always encouraged me to work out problems, and developed my research. In addition, I am most grateful that he allowed me to do what I want to do, and supported whatever I did. This experience cultivated my creativity and proposal ability. I have thought from the bottom of my heart that it is a right thing for me to go on to the doctoral course, which is largely thanks to his respectable character and personality.

I deeply appreciate Professor Yoshiya Fukumoto and Dr. Yusuke Ano for his instructive, expert and enthusiasm advice based on their deeply understanding in chemistry. Through my labolatory life, they helped me in the daily scenes other than research.

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I wish to appreciate Professor Mitsuru Akashi, Professor Toshiyuki Kida, Professor Michiya Matsusaki, Professor Hiroharu Ajiro (Nara Institute of Science and Technology), Professsor Takami Akagi and Dr. Akihiro Nishiguchi (Reasearcher, National Institute for Materials Science) in the once Akashi group. They helped me build the foundation to paly an active part as a researcher, when I was a fourth year undergraduate student.

I express special appreciation to the secretaries in our labolatory, including Ms. Yoshimi Shinomiya and Ms. Junko Ohmagari for their generous assistance.

I would like to express my appreciation to the past and and present members of the Chatani group. The respectable and talented senior menbers: Dr. Takeshi Uemura (Mitusbishi Tanabe Pharma), Dr. Katsuaki Baba (Ono Pharma), Dr. Hirotaka Kinuta (Shionogi Pharma), Dr. Yoshinori Aihara (Sumitomo Dainippon Pharma), Dr. Keisuke Nakamura (TOSOH), Dr. Kaname Shibata (Mitsui Chemicals), Dr. Takayuki Furukawa (Japan Tabacco), Dr. Masaya Hirano (TOSOH) and Dr. Toshifumi Morioka (Mitsubishi Chemicals). Thanks to them, I could spent fruitfull and happy time, and developed my research through discussion with them, especially Dr. Hirotaka Kinuta and Dr. Takayuki Furukawa, who had worked on the similar contents of research to my theme.

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Professor Chatani allowed me to spend a period of time to be engaged in total synthesis in the Brian M. Stoltz group at California Institute of Technology (Caltech) in USA from April to July 2017. It was great and exiting experience not only to deepen my knowledge about chemistry through studying the different research theme from that in the Chatani group but also to touch the culture and customs of the foreign country. I would like to express my sincere gratitude to Professor Brian M. Stoltz for accepting me as a visiting student. In addition, I deeply appreciate Japanese postdoctoral fellows and visiting resarchers in Caltech who helped me in various situations during the research stay: Dr. Kohei Hayashida (Nippon Chemiphar), Dr. Makoto Yoritate (Postdoctoral fellow, UC Berkeley), Mr. Tatsuya Okita (Ishihara Sangyo), Dr. Toshihiko Iwayama (Japan Tabacco), Dr. Yasuaki Nakayama (Postdoctoral fellow, Caltech), Dr. Yusuke Masuda (Kyoto University).

I am grateful for and wish to acknowledge Yoshida Scholarship Foundation for Doctor 21. Thanks to the financial assistance, I could enjoy my research and produce reselts including submitting papers and presenting in many scientific meetings.

At last but not least, I would like to express my thanks to my parents Mr. Shinobu Igarashi and Ms. Hiroe Igarashi for their continuous and kind support.

Suita, Osaka

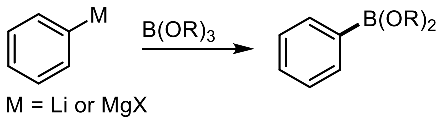
January 2019

Takuya Igarashi

Contents

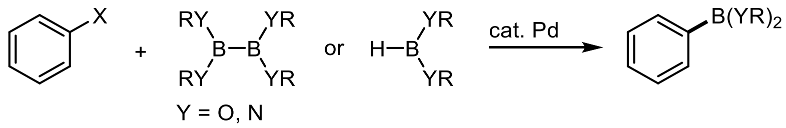
General Introduction

Organoboron reagents are widely used for the construction of carbon-carbon and carbon-heteroatom bonds in modern organic synthesis.[1] They are typically prepared by the reaction of organomagnesium or organolithium reagents with boron electrophiles (**eq. 1**). However, this reaction has poor functional group tolerance because of the strong nucleophilicity of the organometallic reagents that are used in such reactions.



(1)

A catalytic method that does not require the use of strong nucleophiles such as the examples shown above has recently been developed. One of the most useful catalytic methods involves the borylation of aryl halides using organoboron reagents in the presence of a Pd catalyst, a reaction that was first reported by Miyaura and Ishiyama, and which shows a higher functional group tolerance than the method shown in **eq. 1** (**eq. 2**).[2] Another important and commonly used catalytic method is the direct borylation of an inert aromatic C-H bond, which proceeds under mild reaction conditions by using an Ir/bipyridine system developed by Hartwig, Miyaura and Ishiyama (**eq. 3**).[3]



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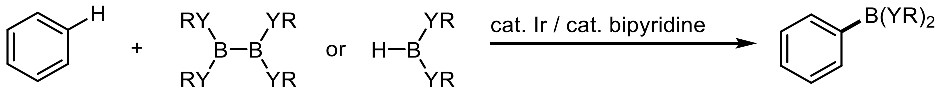
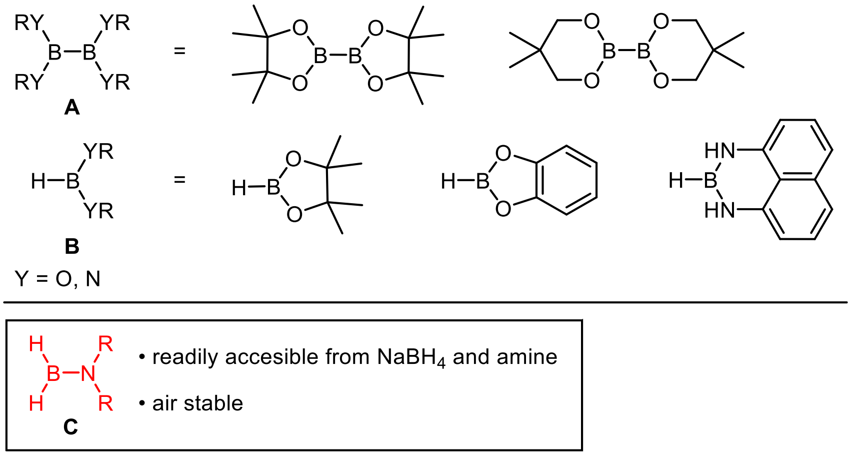


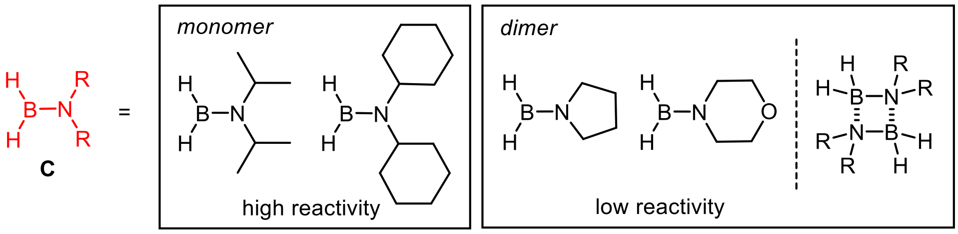
(3)

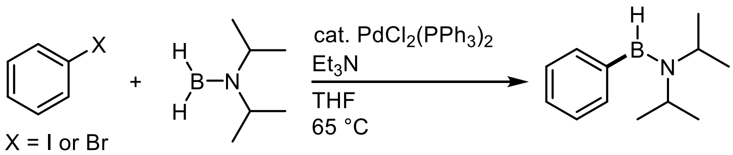
Because they are stable and readily available, diboron **A** and hydroborane **B** derivatives are frequently used as boron reagents in such reactions (**Scheme 1**). Although, like **A** and **B**, the dihydroaminoborane **C** is also stable in air, and can be readily synthesized in two steps from the corresponding amine and $NaBH_4$, **C** has rarely been used in catalytic reactions. The aminoborane **C** was first reported in the 1960s,[4] although catalytic reactions using **C** had not been developed until the 2000s, because **C** typically exists in the form of unreactive cyclic and linear oligomers. In 2003, Alcaraz and co-workers reported that aminoborane reagents bearing a sterically hindered amino group can be isolated in monomeric form as a distillable liquid (**Scheme 2**).[5] This group also utilized diisopropylaminoborane as a borylating reagent of aryl halides in the presence of $PdCl_2(PPh_3)_2$ (**eq. 4**). In 2005, they reported on the use of diisopropylaminoborane in the Pd-catalyzed borylation of alkenyl halides (**eq. 5**).[6] In 2008, a further detailed study of aminoborane reagents was conducted by Singaram and co-workers.[7] They developed a systematic procedure for the synthesis of aminoborane reagents bearing various amino groups, and demonstrated (using ^{11}B NMR spectroscopy) that less sterically hindered aminoborane reagents such as pyrrolidylborane and morpholinoborane exist as dimers (**Scheme 2**). The dimers exist as four-membered cyclic structures that are formed through the coordination of a nitrogen atom to a boron atom. They also showed that dimeric aminoborane reagents are less reactive than monomeric aminoborane reagents in reduction reactions of cyano or ester moieties in the presence of a catalytic amount of $LiBH_4$ (**eq. 6, 7**).

Scheme 1. Commonly Used Boron Reagents for Catalytic Borylation



Scheme 2. Aminoborane Reagents





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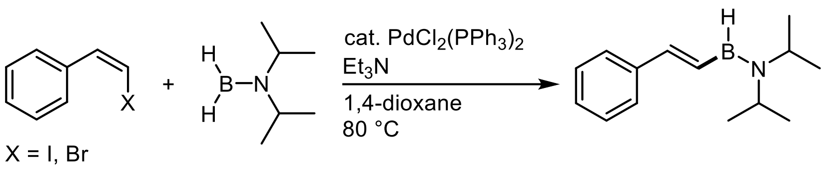

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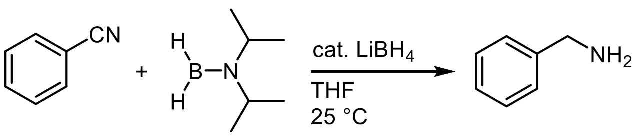

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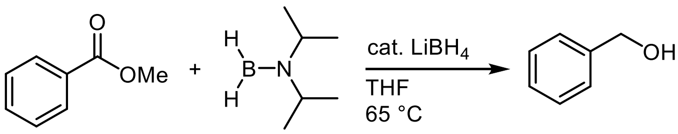
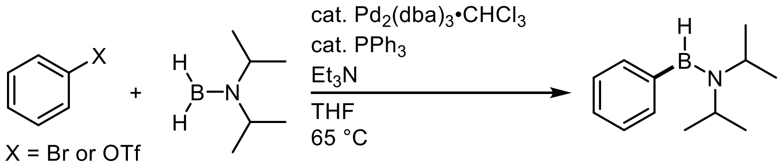


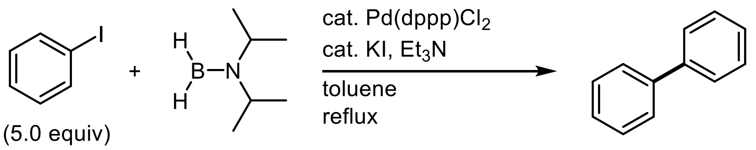
(7)

Since these pioneering works by Alcaraz and Singaram, other examples of the use of diisopropylaminoborane in the catalytic borylation of aryl halides have been reported. In 2011, Singaram and co-workers reported that the borylation of aryl halides using diisopopylaminoborane was accelerated by using a combination of $Pd_2(dba)_3$•$CHCl_3$ and PPh_3, instead of $PdCl_2(PPh_3)_2$ (**eq. 8**).[8] Unlike previously reported methods, the reaction conditions enabled the effective borylation of, not only aryl iodides and bromides but, aryl triflates as well.



(8)

In 2012, Pucheault and co-workers reported that Pd-catalyzed homo-coupling reactions of aryl iodides via borylation using diisopropylaminoborane proceeded in the presence of an excess amount of an aryl iodide (**eq. 9**).[9] They reported on the development of Pd-catalyzed tandem cross-coupling reactions of aryl iodides with the aminoborylated products generated by the borylation of other aryl iodides using diisopropylaminoborane, to give unsymmetrical biaryl derivatives (**eq. 10**).



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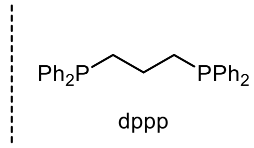
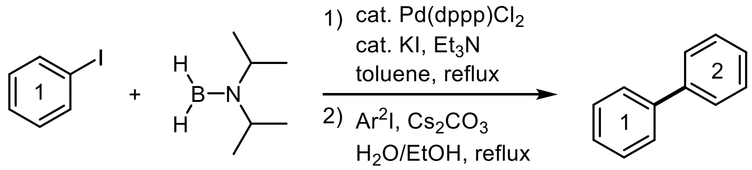
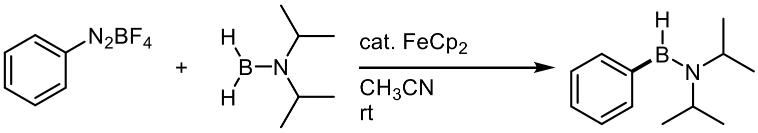




(10)

In 2013, Pucheault and co-workers also reported that diisopropylaminoborane can be used for the Fe-catalyzed borylation of arenediazonium salts at room temperature (**eq. 11**).[10] The tolerance of the aryl iodide and bromide moieties is notable, when considering that the borylation of aryl halides proceeds smoothly when Pd catalysts are used. Hence, unlike previously reported borylation reactions using an aminoborane reagent, this reaction permits iodo- and bromo-substituted aminoborylated compounds to be prepared. Although the reaction proceeded efficiently with 1.0 mol% $FeCp_2$, increasing the amount of $FeCp_2$ was ineffective, indicating that the reaction proceeded via a radical mechanism. In fact, the radical nature of the mechanism was confirmed when cyclization products and no borylated products were formed when the reaction was carried out using the 2-allyloxyphenyldiazonium salt under borylation reaction conditions (**eq. 12**).



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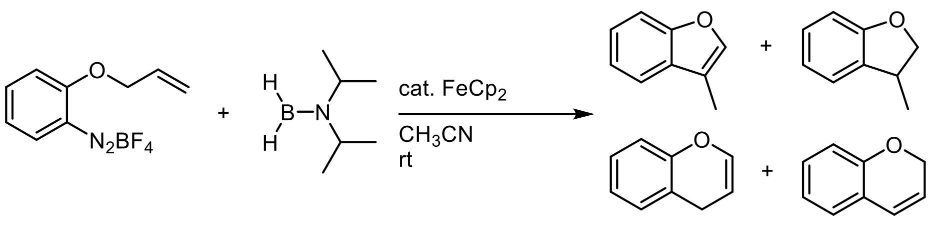
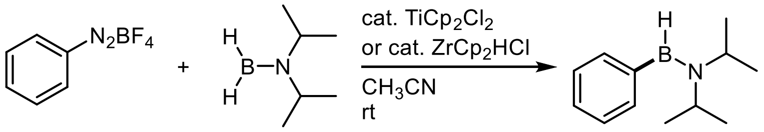


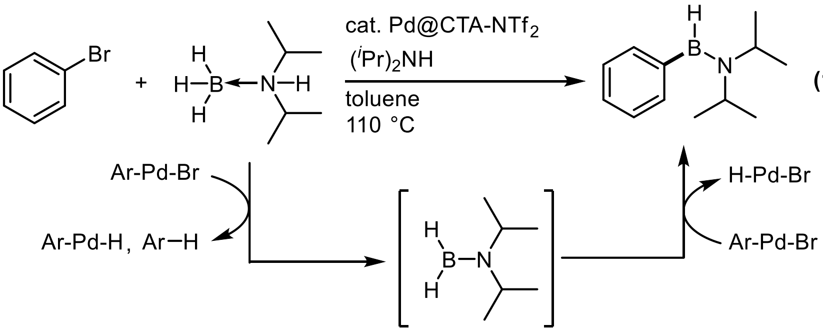
(12)

In 2014, the use of a Ti or Zr complex as a catalyst in the same type of reaction was reported by the same group (**eq. 13**).[11] Interestingly, this reaction did not proceed with the commonly used boron reagents **A** or **B** were used, but only diisipropylaminoborane showed a high reactivity under these reaction conditions.



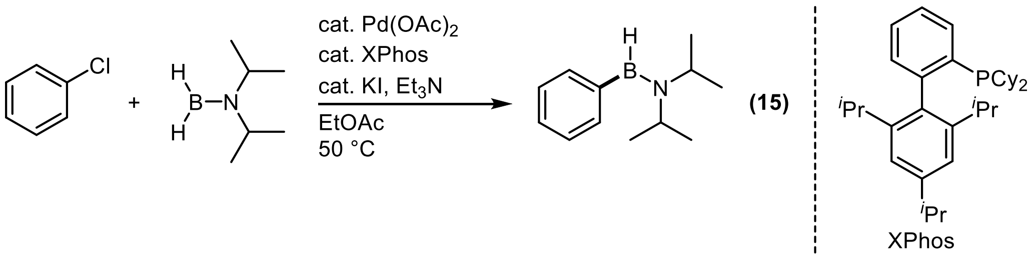
(13)

They also reported sequential dehydrogenation-arylation reactions of the easily accessible and quite stable diisopropylamine-borane complex using aryl bromides catalyzed by a Pd nanoparticle, Pd@CTA-NTf$_2$ (cetyltrimethylammonium triflimide) (**eq. 14**).[12] Although the yields of the borylation products were less than 50% with any aryl bromide, the theoretical yield was limited to 50%, because 0.50 equivalent of the aryl bromide is consumed for the generation of diisopropylaminoborane through the reaction of diisopropylamine-borane complex with the oxidative addition complex Ar-Pd-Br, which releases Ar-H and H-Pd-Br.

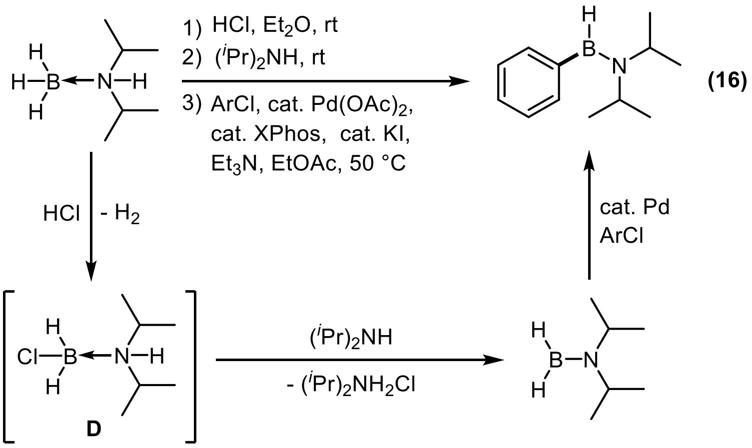


(14)

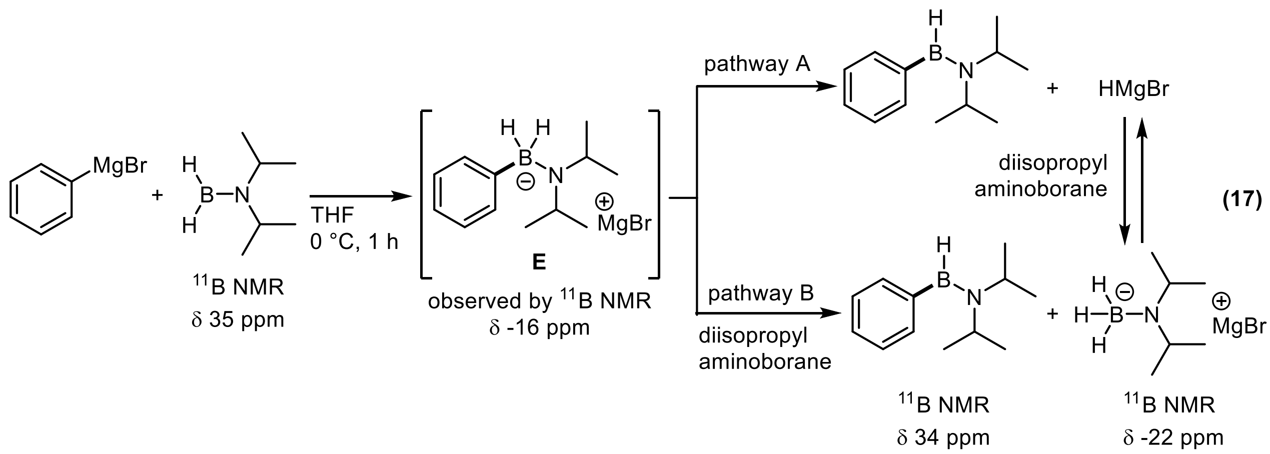
They also reported on the use of diisopropylaminoborane in a Pd/XPhos system[13] in the borylation of aryl chlorides (**eq. 15**).[14] In this reaction, the addition of KI is essential for the reaction to proceed efficiently. The KI was thought to be involved in the transmetallation step of the catalytic cycle, because this reaction was not accelerated when electron-poor aryl chlorides were used as substrates, which suggested that the rate-determining step of this reaction was not the oxidative addition to C-Cl bonds. DFT calculations indicate that, when an aminoborane reagent is used in the borylation of aryl iodides, a Ar-Pd$^+$ species would be generated from the dissociation of the iodide ligand in a Ar-Pd-I complex, which then reacts smoothly with an aminoborane reagent.[15] Based on these results, it is thought that the role of KI is to convert Ar-Pd-Cl to Ar-Pd-I, and promote the formation of a Ar-Pd$^+$ species.



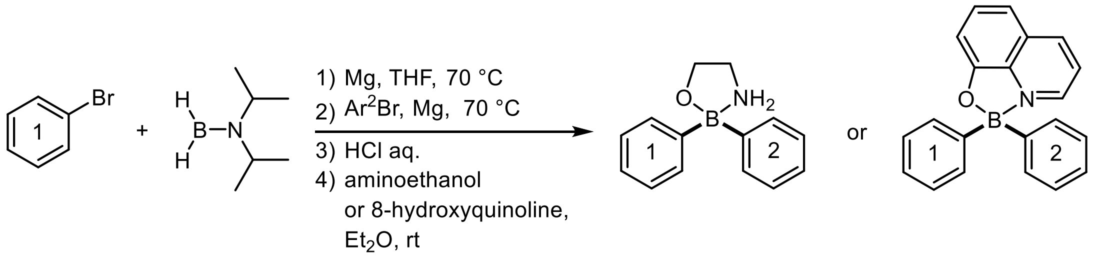
In 2015, the use of an diisopropylamine-borane complex in Pd-catalyzed borylation reactions of aryl halides was reported by Pucheault and co-workers (**eq. 16**).[16] The amine-borane complex is treated by HCl in Et$_2$O to afford the amine-boronium intermediate **D**,[17] followed by (^{i}Pr)$_2$NH, leading to the corresponding aminoborane reagent. This reaction can be applied to aryl triflates, iodides, bromides and chlorides, and can be performed on a multigram scale.



Non-catalyzed reactions using diisopropylaminoborane have also been reported. In 2012, Singaram and co-workers reported on the reaction of diisopropylaminoborane with Grignard reagents to afford aliphatic and aromatic aminoborylated products (**eq. 17**).[18] This reaction proceeds efficiently at 0 °C within 1 h. Although the mechanism is not fully understood, they observed the formation of the bromomagnesium aryl(diisopropylamino)borohydride adduct **E** as an intermediate in this reaction by ^{11}B NMR spectroscopy. The hydride of **E** functions as a leaving group to give the desired borylated product. Hydride elimination from **E** was thought to take place through pathway A or B. They proposed that the reaction proceeds mainly through Pathway A, because only 1.2 equivalents of aminoborane were required to form the aminoborylated product in yields in excess of 95%.

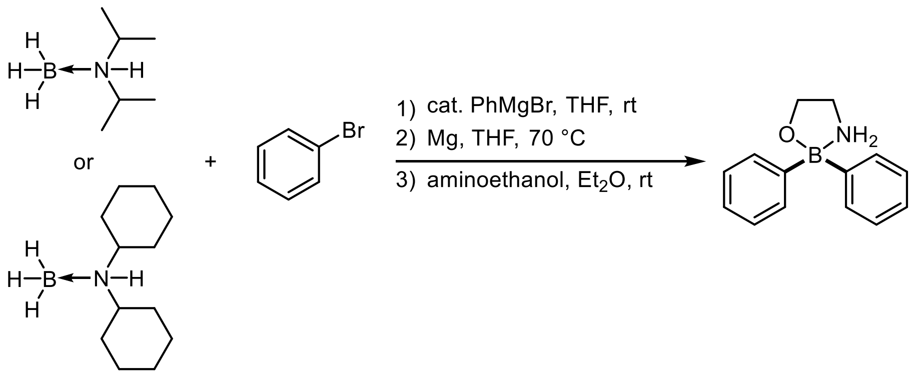


In 2015, Pucheault and co-workers reported on the reaction of phenyl Grignard reagents with both of the two B-H bonds in diisopropylaminoborane to give, not only symmetrical, but also unsymmetrical diarylborinic acids[19] (**eq. 18**).[20] To the best of our knowledge, this is the first reaction in which both of the B-H bonds in an aminoborane reagent are utilized. In addition, they confirmed that the use of phenyl Grignard reagents is essential for the reaction to proceed efficiently, but phenyllithium reagents were found to be ineffective. In this reaction, pure borinic acids were obtained without the need for column chromatography or crystallization. The final products could be isolated by simple filtration as borinate adducts with ethanolamine or 8-hydroxyquinoline. The resulting diarylborinic acid derivatives can be used as the reactants in various types of cross-coupling reactions[21] and organocatalysts.[22, 23]



(18)

In 2017, Pucheault, Pinet and co-workers also reported on the synthesis of diarylborinic acid derivatives by the reaction of aryl bromides with diisopropylamine-borane or dicyclohexylamine-borane complexes in the presence of Mg (**eq. 19**).[24] The reaction of an amine-borane complex with PhMgBr afforded an aminoborohydride **F**, which reacts with an amine-borane complex to afford the corresponding aminoborane (**eq. 20**). This reaction cannot be applied to Grignard reagents that contain CF_3 and NO_2 groups as substituents, because of the stability of arylaminoborohydride intermediates (cf. **E** in **eq. 17**) and the low nucleophilicity of the Grignard reagents.



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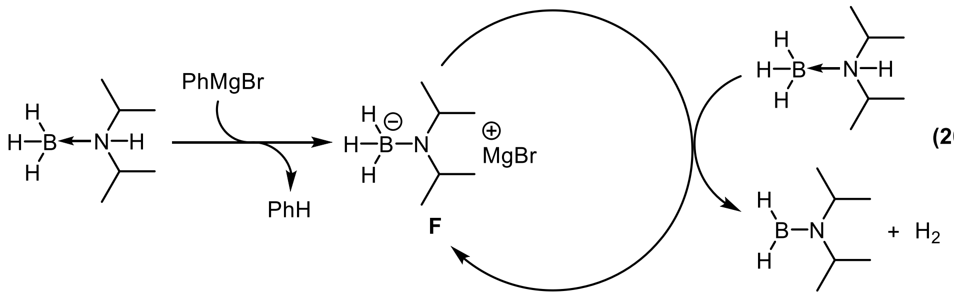
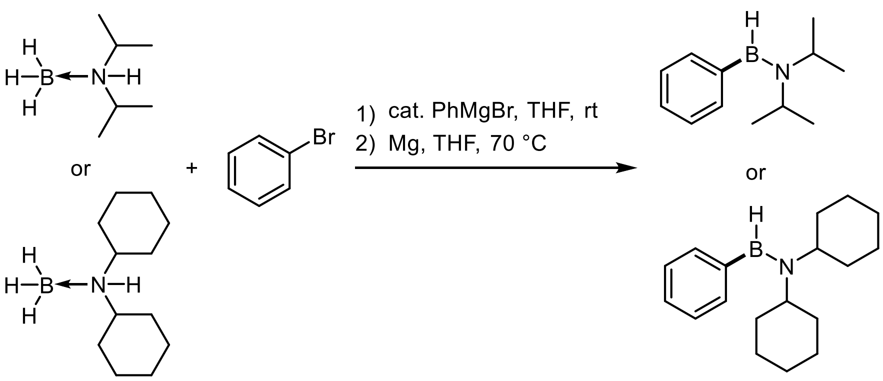


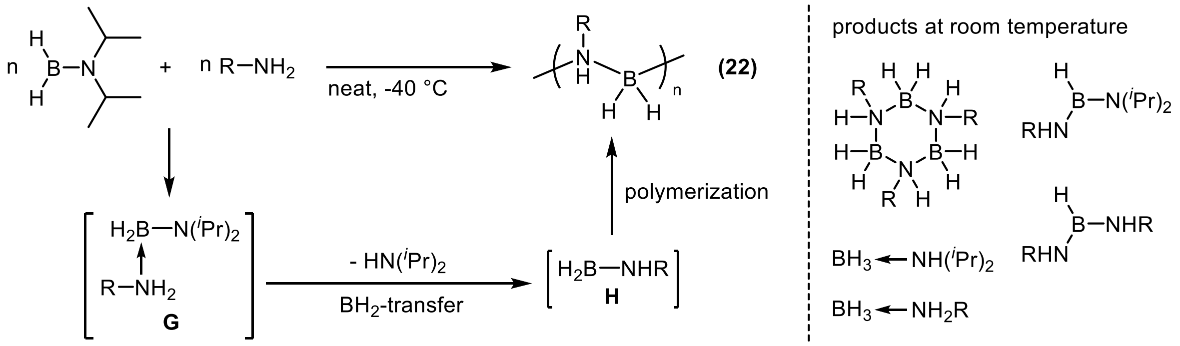
(20)

In 2019, they also reported the boryaltion reactions of aryl halides using diisopropylamine-borane or a dicyclohexylamine-borane complex in the presence of Mg (**eq. 21**).[25] Unlike the previously reported reaction (**eq. 19**), diarylborinic acids were not formed, because of the low loading of Grignard reagents to the amine-borane complex.



(21)

Diisopropylaminoborane has also been utilized for the synthesis of polyaminoborane. Alcaraz and co-workers reported that, at low temperatures, the reaction of diisopropylaminoborane with a variety of primary amines affords high-molecular-weight linear polyaminoborane under solvent-free and metal-free conditions (**eq. 22**).[26] A mixture of cyclotriborazane, diaminoborane and an amine-borane complex were produced when the reaction was carried out at room temperature. In this reaction, diisopropylaminoborane plays the role of an efficient BH_2-transfer reagent via the temporary formation of the amine-diisopropylaminoborane adduct **G**, followed by the elimination of diisopropylamine, leading to the corresponding alkylaminoborane **H** which further polymerizes to afford the desired polyaminoborane.



As discussed thus far, catalytic reactions using diisopropylaminoborane are limited to the catalytic borylation of aryl halides and pseudohalides, and its use in other types of catalytic reactions has not been reported.

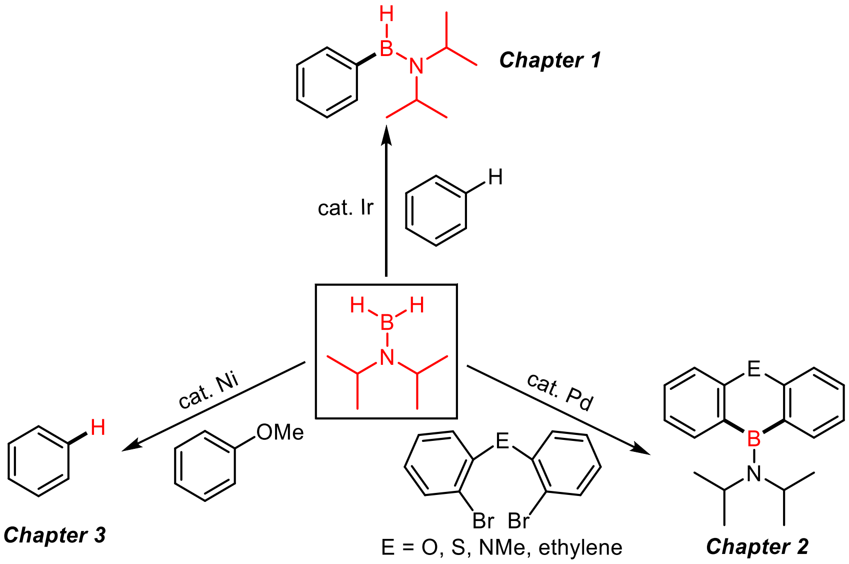
In this study, the use of diisopropylaminoborane in a new type of reaction is reported. This thesis consists of the following three chapters (**Scheme 3**).

In chapter 1, the borylation of aromatic C-H bonds using diisopropylaminoborane by an Ir/*N*-heterocyclic carbene (NHC) ligand is discussed. This is the first demonstration of the use of diisopropylaminoborane in the borylation of aromatic C-H bonds. The resulting aminoborylated intermediates can be converted into various boron products by the treatment with protecting reagents in a one-pot reaction.

In chapter 2, the Pd-catalyzed, two-fold borylation of dihalides using diisopropylaminoborane for the synthesis of cyclic diarylborinic acids is discussed. Catalytic reactions using both of the two B-H bonds of an aminobornane reagent had not reported, because the second B-H bond of an aminoborane reagent is not very reactive. In this reaction, the second borylation successfully proceeds by utilizing an intramolecular process in which an entropic advantage can facilitate this difficult process.

In chapter 3, the Ni-catalyzed reduction of C-O bonds in anisole derivatives using diisopropylaminoborane as a reductant is discussed. The reductive cleavage reactions of anisole derivatives reported here can only be applied to π-extended ethers such as naphthyl and biphenyl skeletons, and cannot be used in reactions involving anisole derivatives. In this study, unlike previously reported reactions, the use of diisopropylaminoborane enables the effective reduction of simple anisole derivatives.

Scheme 3. Catalytic Reactions Using Diisopropylaminoborane



References

(1) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Miyaura, N. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1535. (c) Hall, D. G. *Boronic Acids: Preparation and Applications in Organic Synthesis*, *Medicine and Materials*; Wiley-VCH: Weinheim, Germany, 2011.

(2) Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508.

(3) (a) A review on C(sp^2)-H bond borylation: Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890. (b) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390. (c) Ishiyama, T.; Takagi, J.; Hartwig, J. F.; Miyaura, N. *Angew. Chem. Int. Ed*. **2002**, *41*, 3056.

(4) Köster, V. R.; Bellut, H.; Hattori, S. *Justus Liebigs Ann. Chem.* **1968**, *720*, 1.

(5) Euzénat, L.; Horhant, D.; Ribourdouille, Y.; Duriez, C.; Alcaraz, G.; Vaultier, M. *Chem. Commun.* **2003**, 2280.

(6) Euzénat, L.; Horhant, D.; Brielles, C.; Alcaraz, G.; Vaultier, M. *J. Organomet. Chem.* **2005**, *690*, 2721.

(7) Pasumansky, L.; Haddenham, D.; Clary, J. W.; Fisher, G. B.; Goralski, C. T.; Singaram, B. *J. Org. Chem.* **2008**, *73*, 1898.

(8) Haddenham, D.; Bailey, C. L.; Vu, C.; Nepomuceno, G.; Eagon, S.; Pasumansky, L.; Singaram, B. *Tetrahedron* **2011**, *67*, 576.

(9) Marciasini, L.; Richy, N.; Vaultier, M.; Pucheault, M. *Chem. Commun.* **2012**, *48*, 1553.

(10) Marciasini, L. D.; Richy, N.; Vaultier, M.; Pucheault, M. *Adv. Synth. Catal.* **2013**, *355*, 1083.

(11) Marciasini, L. D.; Vaultier, M.; Pucheault, M. *Tetrahedron Lett.* **2014**, *55*, 1702.

(12) Guerrand, *H. D. S.;* Marciasini, L. D.; Gendrineau, T.; Pascu, O.; Marre, S.; Pinet, S.; Vaultier, M.; Aymonier, C.; Pucheault, M. *Tetrahedron* **2014**, *70*, 6156.

(13) Biarylphosphine ligands have been used in cross-coupling reactions: Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461.

(14) Guerrand, H. D. S.; Marciasini, L. D.; Jousseaume, M.; Vaultier, M.; Pucheault, M. *Chem. Eur. J.* **2014**, *20*,

5573.

(15) Lam, K. C.; Marder, T. B.; Lin, Z. *Organometallics* **2010**, *29*, 1849.

(16) Guerrand, H. D. S.; Vaultier, M.; Pinet, S.; Pucheault, M. *Adv. Synth. Catal.* **2015**, *357*, 1167.

(17) Metters, O. J.; Chapman, A. M.; Robertson, P. M.; Woodall, C. H.; Gates, P. J.; Wass, D. F.; Manners, L. *Chem. Commun.* **2014**, *50*, 12146.

(18) Bailey, C. L.; Murphy, C. L.; Clary, J. W.; Eafon, S.; Gould, N.; Singaram, B. *Heterocycles* **2012**, *86*, 331.

(19) Several synthetic methods of diarylborinic acids using trialkoxyborane reagents have been reported: (a) Povlock, T. P.; Lippincott, W. T. *J .Am. Chem. Soc.* **1958**, *80*, 5409. (b) Chen, X.; Ke, H.; Chen, Y.; Guan, C.; Zou, G. *J. Org. Chem.* **2012**, *77*, 7572. (c) Guan, C.; Huang, L.; Ren, C.; Zou, G. *Org. Process Res. Dev.* **2018**, *22*, 824.

(20) Marciasini, L.; Cacciuttolo, B.; Vaultier, M.; Pucheault, M. *Org. Lett*. **2015**, *17*, 3532.

(21) (a) Winkle, D. D.; Schaab, K. M. *Org. Process Res. Dev.* **2001**, *5*, 450. (b) Li, X.; Feng, Y.; Lin, L.; Zou, G. *J. Org. Chem.* **2012**, *77*, 10991. (c) Chen, X.; Ke, H.; Zou, G. *ACS Catal.* **2014**, *4*, 379. (d) Dimitrijević, E.; Cusimano, M.; Taylor, M. S. *Org. Biomol. Chem.* **2014**, *12*, 1391. (e) HaiHua, K.; XiaoFeng, C.; YuanYuan, F.; Gang, Z. *Sci. China Chem.* **2014**, *57*, 1126. (f) Ke, H.; Chen, X.; Zou, G. *J. Org. Chem.* **2014**, *79*, 7132. (g) Li, X.; Zou, G. *J. Organomet. Chem.* **2015**, *794*, 136. (h) Hubrich, J.; Himmler, T.; Rodefeld, L.; Ackermann, L. *Adv. Synth. Catal.* **2015**, *357*, 474. (i) Zhang, N.; Wang, C.; Zou, G.; Tang, J. *J. Organomet. Chem.* **2017**, *842*, 54. (j) Wang, C.; Zhang, J.; Tang, J.; Zou, G. *Adv. Synth. Catal.* **2017**, *359*, 2514. (k) Guan, C.; Feng, Y.; Zou, G.; Tang, J. *Tetrahedron* **2017**, *73*, 6906. (l) Wang, C.; Huang, L.; Wang, F.; Zou, G. *Tetrahedron* **2018**, *59*, 2299. see also (19b).

(22) Reviews on diarylborinic acid catalyzed reactions: (a) Dimitrijević, E.; Taylor, M. S. *ACS Catal.* **2013**, *3*, 945. (b) Taylor, M. S. *Acc. Chem. Res.* **2015**, *48*, 295.

(23) (a) Lee, D.; Newman, S. G.; Taylor, M. S. *Org. Lett.* **2009**, *11*, 5486. (b) Chudzinski, M. G.; Chi, Y.; Taylor, M. S. *Aust. J. Chem.* **2011**, *64*, 1466. (c) Soeta, T.; Kojima, Y.; Ukaji, Y.; Inomata, K. *Tetrahedron Lett.* **2011**, *52*, 2557. (d) Chan, L.; Taylor, M. S. *Org. Lett.* **2011**, *13*, 3090. (e) Lee, D.; Taylor, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 3724. (f) Gouliaras, C.; Lee, D.; Chan, L.; Taylor, M. S. *J. Am. Chem. Soc.* **2011**, *13*3, 13926. (g) Lee, D.; Taylor, M. S. *Synthesis* **2012**, *44*, 3421. (h) Oishi, S.; Saito, S. *Angew. Chem. Int. Ed.* **2012**, *51*, 5395. (i) Lee, D.; Wikkiamson, C. L.; Chan, L.; Taylor, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 8260. (j) Mcclary, C. A.; Taylor, M. S. *Carbohydr. Res.* **2013**, *381*, 112. (k) Beale, T. M.; Taylor, M. S. *Org. Lett.* **2013**, *15*, 1358. (l) Dimitrijević, E.; Taylor, M. S. *Chem. Sci.* **2013**, *4*, 3298. (m) Beale, T. M.; Moon, P. J.; Taylor, M. S. *Org. Lett.* **2014**, *16*, 3604. (n) Tanveer, K.; Jarrah, K.; Taylor, M. S. *Org. Lett.* **2015**, *17*, 3482. (o) Mancini, R. S.; McClary, C. A.; Anthonipillai, S.; Taylor, M. S. *J. Org. Chem.* **2015**, *80*, 8501. (p) D'Angelo, K. A.; Taylor, M. S. *J. Am. Chem. Soc.* **2016**, *138*, 11058. (q) Garrentt, G. E.; Tanveer, K.; Taylor, M. S. *J. Org. Chem.* **2017**, *82*, 1085. (r) Chardon, A.; Dine, T. M. E.; Legay, R.; Paolis, M. D.; Rouden, J.; Blanchet, J. *Chem. Eur. J.* **2017**, *23*, 2005. (s) Chardon, A.; Maubert, O.; Rouden, J.; Blanchet, J. *ChemCatChem* **2017**, *9*, 4460. (t) D'Angelo, K. A.; Taylor, M. S. *Chem. Commun*. **2017**, *53*, 5978. (u) Slavko, E.; Taylor, M. S. *Chem. Sci.* **2017**, *8*, 7106. (v) Tsuchida, K.; Yuki, M.; Nakajima, K.; Nishibayashi, Y. *Chem. Lett.* **2018**, *47*, 671. (w) Tanveer, K.; Kim, S.-J.; Taylor, M. S. *Org. Lett.* **2018**, *20*, 5327. (x) Wang, G.; Garrett, G. E.; Taylor, M. S. *Org. Lett.* **2018**, *20*, 5375. (y) Izumi, S.; Kobayashi, Y.; Takemoto, Y. *Org. Lett.* **2019**, *21*, 665. (z) Chardon, A.; Rouden, J.; Blanchet, J. *Eur. J. Org. Chem.* **2019**,

995. (a2) Gorelik, D.; Lin, Y. C.; Briceno-Strocchia, A. I.; Taylor, M. S. *J. Org. Chem.* **2019**, *84*, 900.

(24) Richard, J.; Birepinte, M.; Charbonnier, J. B.; Liautard, V.; Pinet, S.; Pucheault, M. *Synthesis* **2017**, *49*, 736.

(25) Marciasini, L. D.; Richard, J.; Cacciuttolo, B.; Sartori, G.; Birepinte, M.; Chabaud, L.; Pinet, S.; Pucheault, M. *Tetrahedron* **2019**, *75*, 164.

(26) Pinheiro, C. A. D. A.; Roiland, C.; Jehan, P.; Alcaraz, G. *Angew. Chem. Int. Ed.* **2018**, *57*, 1519.

Chapter 1

Iridium-Catalyzed Borylation of Aromatic C-H Bonds Using Diisopropylaminoborane

1.1 Introduction

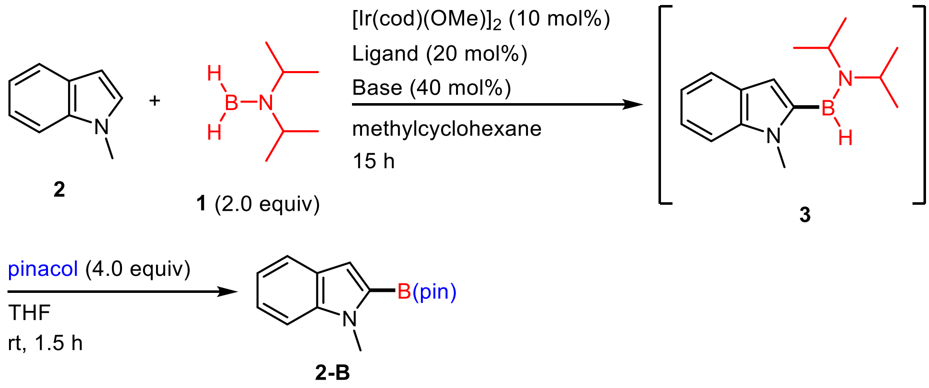
The catalytic borylation of aromatic C-H bonds is an important tool in modern organic synthesis, because it allows the introduction of synthetically useful boron functional groups directly and regioselectively based on steric factors of substrates without the help of any directing groups.[1] Although catalytic systems using various base metals for the borylation of aromatic C-H bonds have been developed, an Ir/bipyridine complex reported by Hartwig and co-workers is the most state-of-the-art.[2] Herrmann and co-workers reported that an Ir/NHC ligand complex is effective in the borylation of aromatic C-H bonds.[3]

Herein, the borylation of aromatic C-H bonds using diisopropylaminoborane **1** in the presence of an Ir/NHC ligand catalyst was investigated.

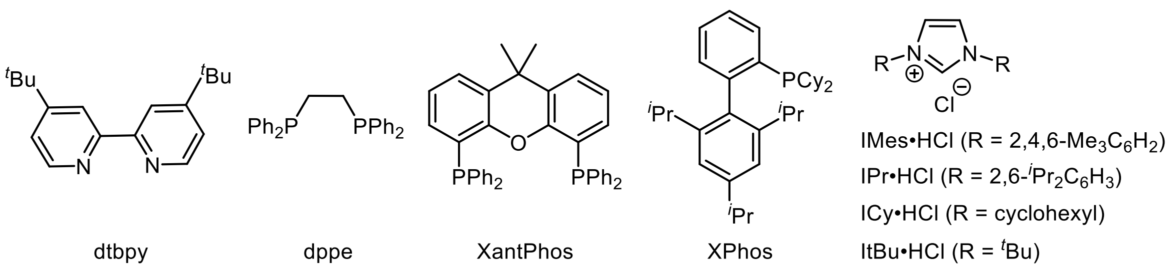
1.2 Results and Discussion

On the basis of a superior reactivity of indoles in several C-H borylation reactions,[4] the author initially examined the borylation of *N*-methylindole **2** with diisopropylaminoborane **1** using an Ir catalyst at 140 °C for 15 h. The crude reaction mixture including the aminoborylated intermediate **3** was treated with pinacol and the yield of the product was estimated by ^{1}H NMR spectroscopy. Using dtbpy, the common and effective ligand for Ir-catalyzed C-H borylation,[2] failed to give **2-B** (Entry 1, **Table 1**). Several mono- and diphosphine ligands were found to be active for the formation of **2-B**, but the yields were up to 21% (Entries 2-6). Among the NHCs examined, 1,3-dicyclohexylimidazol-2-ylidene (ICy)[5] was found to be most effective, affording **2-B** in 33% yield with a 2-/3-borylation ratio of 88:12 (Entry 9). It should be noted that $[Ir(cod)(ICy)_2](CF_3CO_2)$ was previously reported to promote C-H borylation of arenes using HBpin[3]. Further optimization using an ICy ligand determined that decreasing the reaction temperature to 110 °C and shortening the reaction time to 4 h markedly improved the yield of **2-B** (72%) with near complete regioselectivity (99:1) (Entry 12).

Table 1. Effect of the Ligand on the Ir-Catalyzed Borylation of **2** with **1**[a]



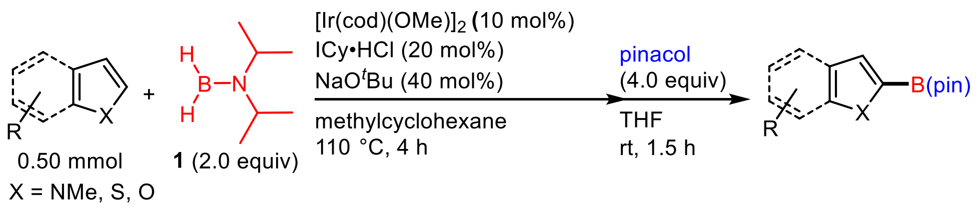
Entry	Ligand	Base	Temp. (°C)	NMR yield[b]	2-isomer/3-isomer
1	dtbpy	none	140	trace	-
2	PPh_3	none	140	21	57/43
3	PCy_3	none	140	3	>99/1
4	dppe	none	140	2	>99/1
5	XantPhos	none	140	18	56/44
6	XPhos	none	140	19	71/29
7	IMes•HCl	NaO^{t}Bu	140	5	>99/1
8	IPr•HCl	NaO^{t}Bu	140	3	>99/1
9	ICy•HCl	NaO^{t}Bu	140	33	88/12
10	I^{t}Bu•HCl	NaO^{t}Bu	140	0	-
11	ICy•HCl	NaO^{t}Bu	110	58	95/5
12[c]	ICy•HCl	NaO^{t}Bu	110	72 (65)[d]	99/1

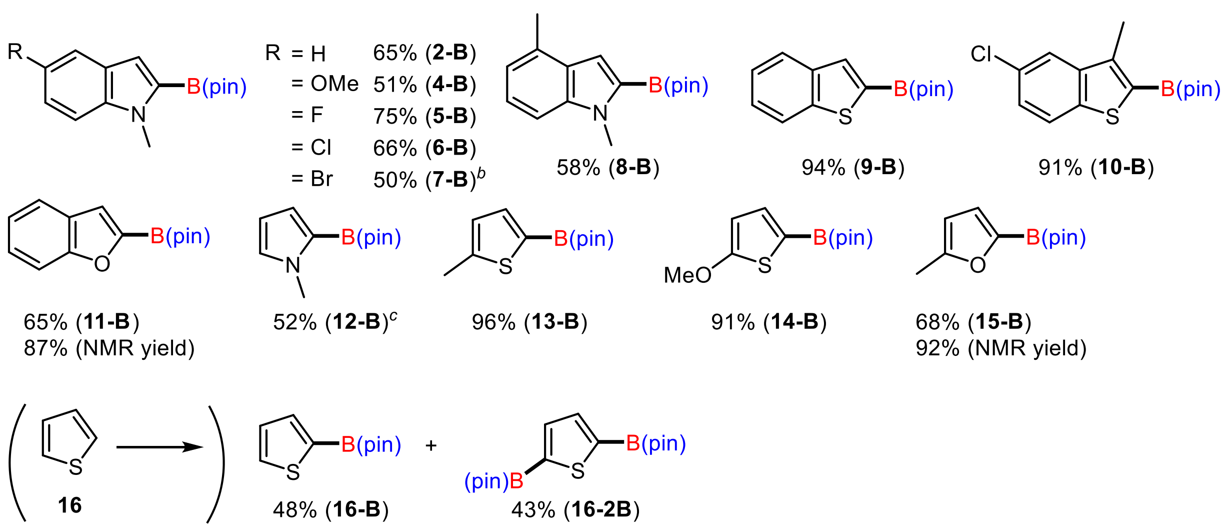


[a] Reaction conditions: **2** (0.50 mmol), **1** (1.0 mmol), $[Ir(cod)(OMe)]_2$ (0.050 mmol), ligand (0.10 mmol), NaO^{t}Bu (0.20 mmol) in methylcyclohexane (1.0 mL) at 140 °C for 15 h. After treatment with pinacol (2.0 mmol), the borylated product was converted to the corresponding pinacolate. [b] The yield refers to a combined NMR yield of 2- and 3-borylated products. [c] Reaction time was shorten to 4 h. [d] Isolated yield.

Having optimized the conditions, the author next examined the scope of Ir/ICy-catalyzed borylation of heteroarene substrates using **1** (**Table 2**). Functionalized indoles, such as those bearing methoxy, fluoro, chloro and bromo groups, all underwent the borylation to form the corresponding 2-borylated products **4-B**, **5-B**, **6-B** and **7-B**, respectively. When 1,4-dimethylindole was used as a substrate, 2-borylated product **8-B** was formed exclusively with no borylation occurring at the benzylic position[6]. Benzothiophenes readily gave 2-borylated products using my catalytic system, as exemplified by the high yields obtained from **9** and **10**. Although benzofuran **11** was also borylated at the 2-position efficiently, the isolated yield was somewhat lower than the yield calculated from the ^{1}H NMR data, probably because of the instability of **11-B** during isolation. My protocol was able to borylate non-benzofused five-membered heteroarenes. Pyrrole **12** was much less reactive than indoles, and required neat conditions to obtain a modest yield of the borylated product **12-B**. 2-Substituted thiophene **13, 14** and furan **15** were borylated successfully at the 6-positions. Thiophene **16** afforded a 1.1:1 mixture of 2-borylated and 2,5-diborylated products under my standard conditions. Electron-deficient heteroarenes such as pyridine and quinolone failed to form the borylated product under the current conditions.

Table 2. Scope of the Heteroarene Substrates[a]

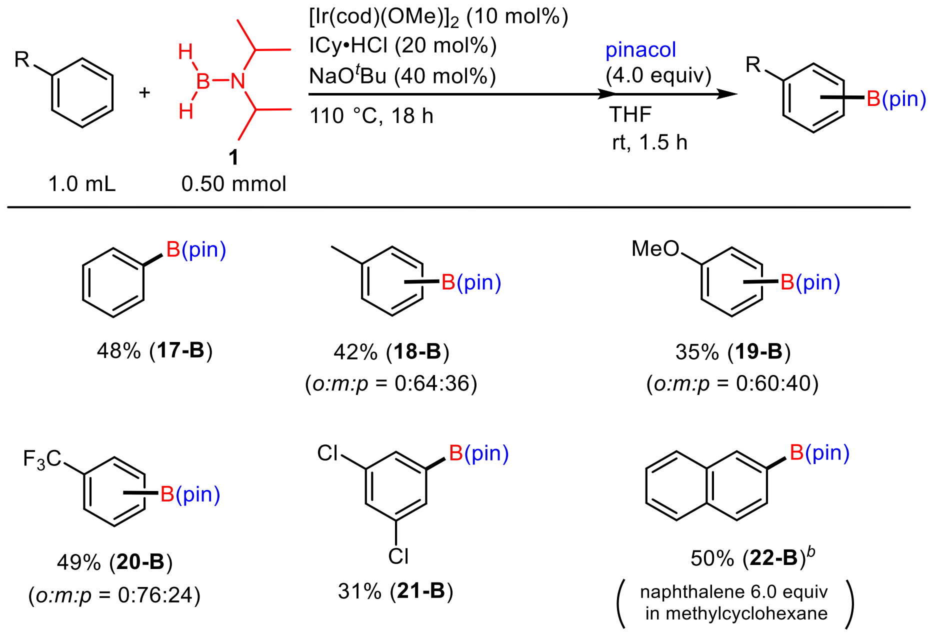




[a] Reaction conditions: heteroarene (0.50 mmol), **1** (1.0 mmol), $[Ir(cod)(OMe)]_2$ (0.050 mmol), ICy·HCl (0.10 mmol), NaO^{t}Bu (0.20 mmol) in methylcyclohexane (1.0 mL) at 110 °C for 4 h. After treatment with pinacol (2.0 mmol), the borylated product was converted to the corresponding pinacolate. [b] Debrominative borylation also occurred with a yield of 6%. [c] Run using 1.0 mL of *N*-methylpyrrole instead of methylcyclohexane.

The author next turned my attention to the borylation reaction of benzene derivatives as substrates (**Table 3**). Unfortunately, benzene derivatives proved to be much less reactive than heteroarenes. For example, Ir/ICy-catalyzed borylation of benzene **17** with **1** afforded **17-B** in 48% isolated yield even when the reaction was conducted under neat conditions. Borylation was relatively independent of the electronic nature of the arene substrates, as indicated by the similar yields and regioselectivity observed with toluene **18**, anisole **19** and trifluoromethylbenzene **20**. Similar to the reported C-H borylation using other boron sources, 1,3-disubstituted benzenes were borylated at the 5-position in a regioselective manner. For example, 1,3-dichlorobenzene **21** was borylated at the 5-position to afford only one product **21-B**. Naphthalene **22** also underwent borylation with **1** at the less hindered 2-position to give **22-B**.

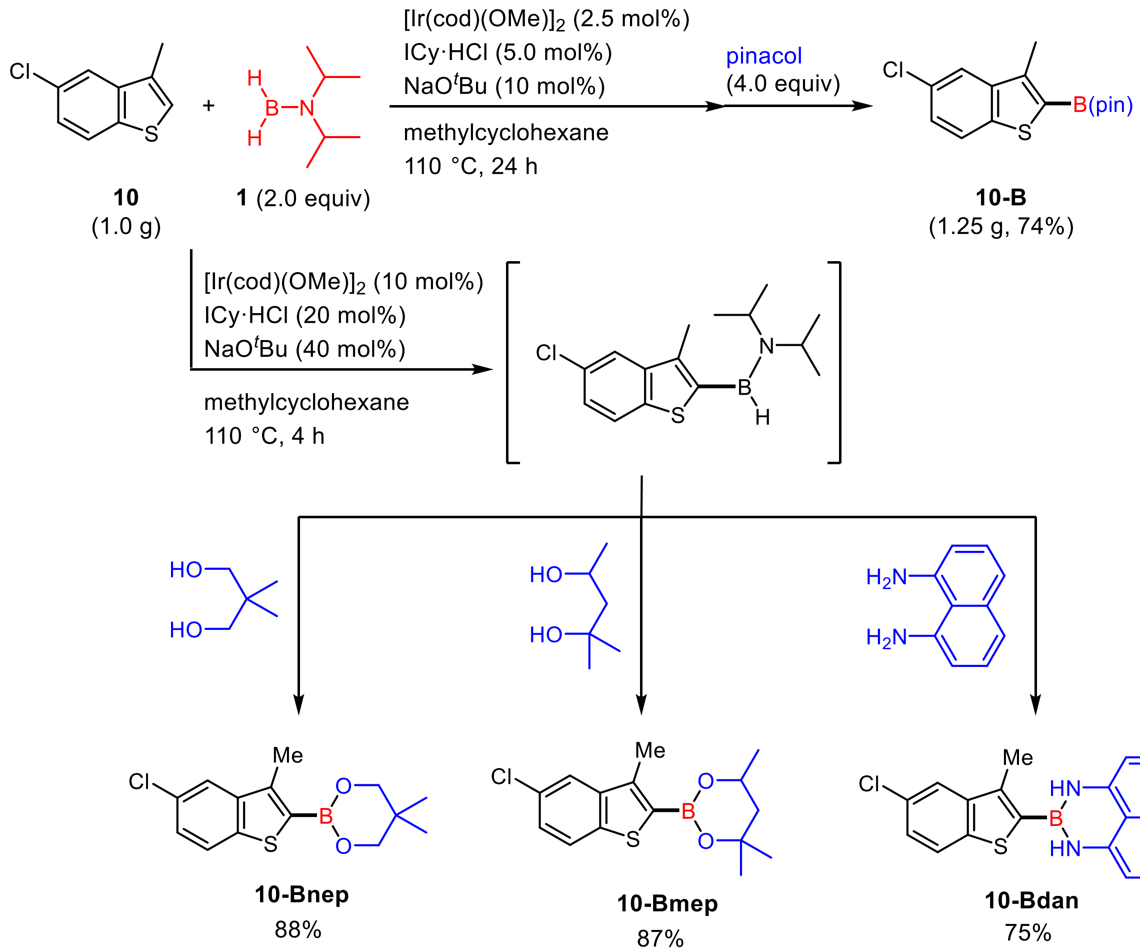
Table 3. Scope of the Arene Substrates[a]



[a] Reaction conditions: arene (1.0 mL), **1** (0.50 mmol), $[Ir(cod)(OMe)]_2$ (0.050 mmol), ICy·HCl (0.10 mmol), NaO^{t}Bu (0.20 mmol) at 110 °C for 15 h. After treatment with pinacol (2.0 mmol), the borylated product was converted to the corresponding pinacolate. [b] Naphthalene (3.0 mmol) was used in methylcyclohexane (1.0 mL).

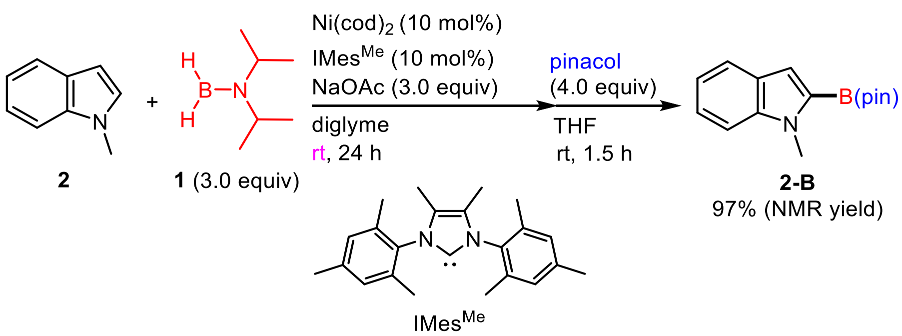
My protocol can be performed on a gram scale without any difficulty using a lower loading of the Ir catalyst (**Scheme 1**, top). Using **1** as the boron source in C-H borylation reactions has the synthetic advantage of allowing various substituents to be introduced onto the boron atom during the work-up stage simply by changing the protecting reagents added (**Scheme 1**, bottom). For example, the addition of different diols afforded the corresponding boronic esters **10-Bnep** and **10-Bmep**.[7] It was also possible to introduce Suginome's dan group (**10-Bdan**),[8] which allows to use the borylated products in more elaborate manners, such as iterative cross-couplings.[9]

Scheme 1. Scalability and Derivatization



The borylation reaction of aromatic C-H bonds with **1** as a boron source also proceeded using a Ni catalyst,[10] instead of an Ir catalyst (**Scheme 2**). The borylation reaction of *N*-methylindole **2** gave **2-B** successfully even at room temperature using a Ni/IMes^{Me} catalytic system. The optimization of this reaction is ongoing.

Scheme 2. Ni-Catalyzed Borylation of **2** with **1**[a]



[a] Reaction conditions: **2** (0.10 mmol), **1** (0.30 mmol), Ni(cod)$_2$ (0.010 mmol), IMes^{Me} (0.010 mmol), NaOAc (0.30 mmol) in diglyme (0.05 mL) at rt for 24 h. After treatment with pinacol (0.50 mmol), the borylated product was converted to the corresponding pinacolate.

1.3 Conclusion

The author has developed an Ir/NHC complex-catalyzed C-H borylation of aromatic substrates using disopropylaminoborane **1** as a borylating reagent. This is the first example of C-H borylation using an aminoborane reagent. The use of an Ir catalyst in conjunction with ICy ligand and **1** resulted in effective catalysts for the borylation of a wide range of C-H bonds in arenes and heterarenes. Notably, the initially formed aminoborylated products can readily be converted into various organoboron compounds bearing various boron-protecting groups just by changing the added protecting reagents.

1.4 Experimental Section

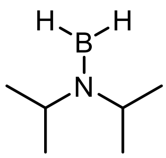
1.4.1 General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL ECS-400 spectrometer in $CDCl_3$ or C_6D_6 with tetrachloroethane as the internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, and m = multiplet), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained using a JASCO FT/IR-4200 spectrometer; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra and high resolution mass spectra (HRMS) were obtained on a JEOL JMS-700 spectrometer. Analytical gas chromatography (GC) was carried out on a Shimazu GC-2014 gas chromatograph, equipped with a flame ionization detector. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with SiO_2 (silicycle SilicaFlash F60 (230-400 mesh)).

1.4.2 Materials

$[Ir(cod)(OMe)]_2$ (TCI), ICy•HCl (TCI) and NaO^{t}Bu (TCI) were used as received. Methylcyclohexane was purified by distillation prior to use. **2** (TCI), **9** (TCI), **10** (TCI), **11** (TCI), **12** (TCI), **13** (TCI), **14** (TCI), **15** (TCI) and **16** (TCI) were obtained from commercial suppliers and used as received. All arenes (TCI) and **22** (Aldrich) were used as received. The other *N*-methylindoles used in this study were synthesized by the reaction of the corresponding indole with MeI according to the literature procedure.[11]

Diisopropylaminoborane (1). [CAS: 22092-92-8]



1

1 was prepared as described in literatures.[12]

To a stirred solution of diisopropylamine (28.2 mL, 200 mmol, 1.0 equiv) in THF (70 mL) were added at 0 °C, H_2SO_4 (5.4 mL, 100 mmol, 0.5 equiv). A white precipitate appeared immediately. After 30 min at 0 °C, were carefully added $NaBH_4$ (8.2 g, 220 mmol, 1.1 equiv). The mixture was allowed to warm to room temperature and stirred for 4 h. The crude was concentrated under vacuum and the residue was taken with toluene (100 mL), washed with water (4 × 100 mL). The organic phase was dried by using Na_2SO_4 and concentrated under reduced pressure to give the amine-borane complex as colorless oil.

The amine-borane complex was refluxed at 195 °C for 9 h, and the **1** was distilled under N_2 to give 17.2 g (76% yield).

1.4.3 General Procedures for Ir-Catalyzed Borylation of Aromatic C-H Bonds Using 1

Method A: Procedure for the Ir-Catalyzed Borylation of Heterocycles Using 1

In a glovebox, $[Ir(cod)(OMe)]_2$ (33.1 mg, 0.050 mmol, 0.10 equiv), ICy•HCl (26.2 mg, 0.10 mmol, 0.20 equiv), NaO^{t}Bu (19.2 mg, 0.20 mmol, 0.40 equiv) and methylcyclohexane (1.0 mL) were added to a 10 mL-sample vial with Teflon-sealed screwcap, and stirred for 5 min at room temperature. A heterocycle (0.50 mmol, 1.0 equiv) and **1** (113.1 mg, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 110 °C for 4 h. After the reaction mixture was cooled to room temperature, the pinacol (236 mg, 2.0 mmol) in THF (2.0 mL) was added and stirred for 1.5 h at room temperature under N_2. The crude mixture was filtered through a pad of Celite eluting with AcOEt. The filtrate was concentrated in vacuo and analyzed by ^{1}HNMR using 1,2-dichloroethane as an internal standard. The crude mixture was concentrated under reduced pressure again, and purified by flash column chromatography over silica gel eluting with Hexane/AcOEt solution. The filtrate was concentrated in vacuo to give a pure borylated product.

Method B: Procedure for the Ir-Catalyzed Borylation of Arenes Using 1

In a glovebox, $[Ir(cod)(OMe)]_2$ (33.1 mg, 0.050 mmol, 0.10 equiv), ICy•HCl (26.2 mg, 0.10 mmol, 0.20 equiv), NaO^{t}Bu (19.2 mg, 0.20 mmol, 0.40 equiv) and benzene (1.0 mL) were added to a 10 mL-sample vial with Teflon-sealed screwcap, and stirred for 5 min at room temperature. **1** (113.1 mg, 0.10 mmol, 2.0 equiv) was then added, and the cap was applied to seal the vial. The vial was stirred at 110 °C for 18 h. After the reaction mixture was cooled to room temperature, the pinacol (236 mg, 2.0 mmol) in THF (2.0 mL) was added and stirred for 1.5 h at room temperature under N_2. The crude mixture was filtered through a pad of Celite eluting with an internal standard. The crude

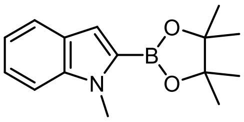
mixture was concentrated under reduced pressure again, and purified by flash column chromatography over silica gel eluting with Hexane/AcOEt solution. The filtrate was concentrated in vacuo to give a pure borylated product.

1.4.4 A procedure for the Gram Scale Synthesis of 2-Borylated 10

In a glovebox, $[Ir(cod)(OMe)]_2$ (91.0 mg, 0.138 mmol, 0.025 equiv), ICy•HCl (73.8 mg, 0.275 mmol, 0.050 equiv), NaO^{t}Bu (52.8 mg, 0.55 mmol, 0.10 equiv) and methylcyclohexane (11.0 mL) were added to a 200 mL-sample vial with Teflon-sealed screwcap, and stirred for 5 min at room temperature. **10** (1.00 g, 5.50 mmol, 1.0 equiv) and **1** (1.24g, 11.0 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 110 °C for 24 h. After the reaction mixture was cooled to room temperature, pinacol (2.57 g, 22.0 mmol, 4.0 equiv) in THF (16 mL) was added and stirred for 1.5 h at room temperature under N_2. The crude mixture was filtered through a pad of Celite eluting with AcOEt. The filtrate was concentrated in vacuo and analyzed by ^{1}HNMR using 1,2-dichloroethane as an internal standard. The crude mixture was concentrated under reduced pressure again, and purified by flash column chromatography over silica gel eluting with Hexane/AcOEt (40/1) solution. The filtrate was concentrated in vacuo to give **10-B** as a white solid (1.25 g, 74%).

1.4.5 Spectroscopic Data for Products

1-Methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (2-B). [CAS: 596819-10-2]



Method A was used. R_f 0.14 (Hexane/EtOAc =20/1). White solid (83 mg, 65%).

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.12 (s, 12H), 3.69 (s, 3H), 7.13 (d, J = 7.8 Hz, 2H), 7.27 (td, J = 0.9, 7.8 Hz, 1H), 7.57 (s, 1H), 7.68-7.70 (m, 1H).

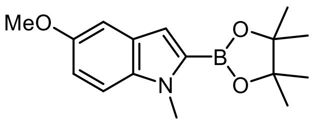
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ1.37 (s, 12H), 3.98 (s, 3H), 7.07-7.10 (m, 1H), 7.14 (s, 1H), 7.24-7.28 (m, 1H), 7.35 (d, J = 8.2 Hz, 1H), 7.64 (d, J = 8.2 Hz, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.9, 32.1, 83.6, 110.1, 115.6, 119.9, 122.2, 123.6, 128.8, 140.9.

HRMS (EI): Calcd for $C_{15}H_{20}BNO_2$ 257.1587, Found 257.1585.

^{1}H NMR spectroscopic data was in agreement with the reported value.[4b]

5-Methoxy-1-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (4-B). [CAS: 1256360-41-4]



Method A was used. R_f 0.057 (Hexane/EtOAc = 40/1). White solid (69 mg, 48%).

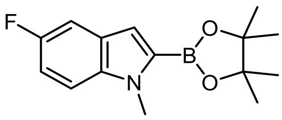
^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.13 (s, 12H), 3.45 (s, 3H), 3.68 (s, 3H), 6.99 (d, J = 9.2 Hz, 1H), 7.08 (d, J = 2.6 Hz, 1H), 7.19 (d, J = 2.6 Hz, 1H), 7.56 (s, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.9, 30.1, 32.2, 55.2, 83.6, 102.4, 110.9, 114.9, 115.4, 136.53, 154.9.

HRMS (EI): Calcd for $C_{16}H_{22}BNO_3$ 287.1693, Found 257.1695.

^{1}H NMR spectroscopic data was in agreement with the reported value[3].

5-Fluoro-1-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (5-B). [CAS: 1683582-67-3]



Method A was used. R_f 0.085 (Hexane/EtOAc = 40/1). White solid (103 mg, 75%).

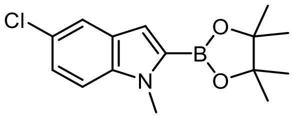
^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.10 (s, 12H), 3.57 (s, 3H), 6.79 (dd, J = 4.1, 9.2 Hz, 1H), 7.00 (dt, J = 2.3, 9.2 Hz, 1H), 7.28 (dd, J = 2.3, 9.6 Hz, 1H), 7.36 (s, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.8, 32.2, 83.7, 106.3 (d, J = 23 Hz), 110.8 (d, J = 9.5 Hz), 112.2 (d, J = 27 Hz), 115.1 (d, J = 4.8 Hz), 128.7 (d, J = 9.5 Hz), 137.5, 158.5 (d, J = 234 Hz).

HRMS (EI): Calcd for $C_{15}H_{20}BFNO_2$ 276.1568, Found 276.1570.

^{1}H NMR spectroscopic data was in agreement with the reported value[3].

5-Chloro-1-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (6-B).



Method A was used. After purification by flush column chromatography over silica gel, a mixture of a borylated product and **6** were obtained (**6-B**: 66%, **6**: 22%; isolated yields). GC/MS analysis revealed the existence of **6-B** and **6**; **6-B** had an m/z of 291 (M^+), and **6** had an m/z of 165 (M^+). The identity and ratio of each of these was determined by the obtained the ^{1}HNMR spectrum of a mixture. The resonances specific to each isomer are as follows: ^{1}H NMR (C_6D_6, 399.78 MHz): δ 0.454 (s, 3H, **6**), 3.52 (s, 3H, **6-B**).

R_f 0.086 (Hexane/EtOAc = 40/1). White solid (**6-B** = 96 mg). Mp = 111 °C.

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.10 (s, 12H), 3.52 (s, 3H), 6.76 (d, 1H, *J* = 8.8 Hz), 7.23 (dd, *J* = 2.0, 8.7 Hz, 1H), 7.33 (s, 1H), 7.60 (d, *J* = 1.9 Hz, 1H).

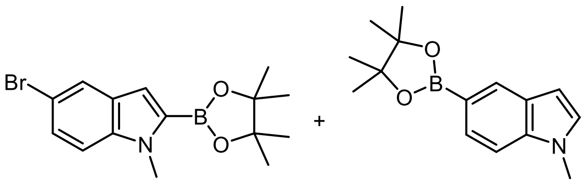
^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.8, 32.1, 83.8, 111.1, 114.8, 121.4, 123.9, 125.7, 129.5, 139.0.

IR (ATR): 2977 w, 2927 w, 2361 m, 2339 w, 1735 w, 1649 w, 1558 w, 1526 m, 1438 w, 1361 s, 1306 s, 1264 m, 1208 w, 1137 s, 1106 m, 1077 m, 1030 m, 974 w, 949 w, 866 m, 849 s, 805 m, 780 w, 732 w, 692 w, 671m.

MS m/z (% relative intensity): 293 (32), 292 (24), 291 (M^+, 100), 290 (25), 218 (12), 209 (18), 208 (17), 207 (10), 206 (31), 205 (12), 193 (12), 192 (21), 191 (35), 190 (22).

HRMS (EI): Calcd for $C_{15}H_{19}BClNO_2$ 291.1197, Found 291.1204.

5-Bromo-1-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (7-B) [CAS: 1192037-87-8] **and 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (7-B').** [CAS: 837392-62-8]



7-B (50%) **7-B'** (6%)

Method A was used. After purification by flush column chromatography over silica gel, a mixture of two borylated products and **7** were obtained (**7-B**: 50%, **7-B'**: 6%, **7**: 20%; isolated yields). GC/MS analysis revealed the existence of two borylated products and **7**; **7-B** had an m/z of 335 (M^+), **7-B'** had an m/z of 257 (M^+), and **7** had an m/z of 209 (M^+). The identity and ratio of each of these was determined by the obtained the ^{1}HNMR spectrum of a mixture. The resonances specific to each isomer are as follws: ^{1}H NMR (C_6D_6, 399.78 MHz): δ 2.74 (s, 3H, **7**), 3.50 (s, 3H, **7-B**), 3.69 (s, 3H, **7-B'**).

MS m/z (% relative intensity) **7-B**: 338 (16), 337 (99), 336 (39), 335 (M^+, 100), 334 (23), 255 (15), 253 (15), 252 (25), 251 (11), 250 (22), 237 (24), 236 (24), 235 (27), 234 (14), 183 (11), 156 (10).

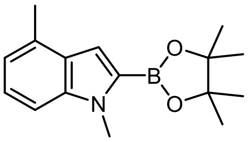
7-B': 258 (18), 257 (M^+, 100), 256 (25), 184 (21), 175 (21), 172 (31), 158 (15), 157 (36), 156 (25).

HRMS (EI) **7-B**: Calcd for $C_{15}H_{19}BBrNO_2$ 335.0692, Found 335.0689.

7-B': Calcd for $C_{15}H_{20}BNO_2$ 257.1587, Found 257.1583.

^{1}H NMR spectroscopic data was in agreement with the reported value.[13]

1,4-Dimethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (8-B).



Method A was used. R_f 0.14 (Hexane/EtOAc = 40/1). White solid (69 mg, 51%). Mp = 151 °C.

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.14 (s, 12H), 2.51 (s, 3H), 3.71 (s, 3H), 6.97 (d, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 7.25 (t, *J* = 8.2 Hz, 1H), 7.64 (s, 1H).

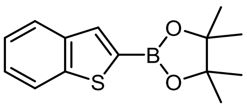
^{13}C NMR (C_6D_6, 100.53 MHz): δ 18.8, 24.9, 32.3, 83.6, 107.9, 114.3, 120.1, 124.0, 128.8, 131.4, 140.8.

IR (ATR): 2975 w, 2921 w, 2361 w, 1606 w, 1580 w, 1522 m, 1496 w, 1467 w, 1383 m, 1349 w, 1317 m, 1293 m, 1258 m, 1239 m, 1216 w, 1139 m, 1111 w, 1070 m, 964 w, 858 m, 827 w, 805 w, 770m , 739 m, 688 m, 670 w.

MS m/z (% relative intensity): 272 (18), 271 (M^+, 100), 270 (25), 198 (16), 189 (29), 188 (11), 172 (10), 171 (29), 170 (24).

HRMS (EI): Calcd for $C_{16}H_{22}BNO_2$ 271.1744, Found 271.17430.

2-(Benzo[*b*]thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (9-B). [CAS：376584-76-8]



Method A was used. R_f 0.086 (Hexane/EtOAc = 40/1). White solid (122 mg, 94%).

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.10 (s, 12H), 7.01-7.09 (m, 2H), 7.54-7.58 (m, 2H), 8.06 (s, 1H).

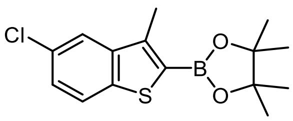
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.38 (s, 12H), 7.35-7.39 (m, 2H), 7.85-7.92 (m, 3H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.8, 84.3, 124.4, 124.7, 122.9, 125.6, 135.3, 141.0, 144.4.

HRMS (EI): Calcd for $C_{14}H_{17}BO_2S$ 260.1042, Found 260.1040.

^{1}H NMR spectroscopic data was in agreement with the reported value.[4d]

2-(5-Chloro-3-methylbenzo[*b*]thiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (10-B).
[CAS：1809298-96-1]



Method A was used. R_f 0.22 (Hexane/EtOAc = 40/1). White solid (140 mg, 91%).

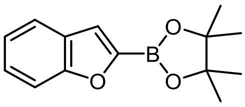
^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.07 (s, 12H), 2.51 (s, 3H), 7.04 (dd, *J* = 1.8, 8.7 Hz, 1H), 7.18 (d, *J* = 8.7 Hz, 1H), 7.63 (d, *J* = 1.8 Hz, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 14.0, 24.8, 84.1, 122.7, 124.0, 126.1, 130.5, 141.9, 142.9, 143.4.

HRMS (EI): Calcd for $C_{15}H_{18}BClO_2S$ 308.0809, Found 308.0811.

^{1}H NMR spectroscopic data was in agreement with the reported value.[4d]

2-(Benzofuran-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (11-B). [CAS: 402503-13-3]



Method A was used. R_f 0.057 (Hexane/EtOAc = 40/1). White solid (79 mg, 65%).

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.08 (s, 12H), 6.98-7.08 (m, 2H), 7.34-7.36 (m, 1H), 7.40-7.42 (m, 1H), 7.48 (d, *J* = 0.92 Hz, 1H).

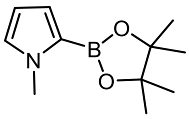
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.39 (s, 12H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.34 (td, 0.9, *J* = 8.2 Hz, 1H), 7.40 (s, 1H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.63 (1H, *J* = 7.8 Hz, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.8, 84.4, 112.1, 120.1, 122.2, 123.0, 126.3, 158.3. One carbon peak is overlapped with solvent peaks.

HRMS (EI): Calcd for $C_{14}H_{17}BO_3$ 244.1271, Found 244.1276.

^{1}H NMR spectroscopic data was in agreement with the reported value.[4d]

1-Methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrrole (12-B). [CAS：850567-47-4]



Method B was used except that the reaction was conducted in *N*-methyl pyrrole (1.0 mL).

R_f 0.14 (Hexane/EtOAc = 40/1). White solid (52 mg, 50%).

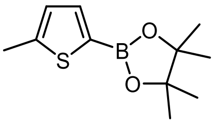
^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.11 (s, 12H), 3.52 (s, 3H), 6.30 (dd, *J* = 1.4, 2.3 Hz, 1H), 7.22 (t, *J* = 1.8 Hz, 1H), 7.33 (dd, *J* = 1.4, 2.3 Hz, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.9, 36.3, 83.0, 109.2, 123.4. One carbon peak is overlapped with solvent peaks.

HRMS (EI): Calcd for $C_{11}H_{18}BNO_2$ 207.1431, Found 207.1431.

^{1}H NMR spectroscopic data was in agreement with the reported value[3].

4,4,5,5-Tetramethyl-2-(5-methylthiophen-2-yl)-1,3,2-dioxaborolane (13-B). [CAS: 476004-80-5]



Method A was used. R_f 0.14 (Hexane/EtOAc = 40/1). Colorless oil (108 mg, 96%).

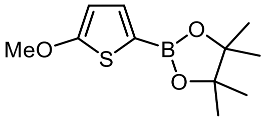
^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.09 (s, 12H), 2.11 (s, 3H), 6.62 (d, *J* = 3.3 Hz, 1H), 7.8 (d, *J* = 3.5 Hz, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 15.1, 24.9, 83.9, 127.5, 138.4, 147.8.

HRMS (EI): Calcd for $C_{11}H_{17}BO_3S$ 208.1271, Found 208.1272.

^{1}H NMR spectroscopic data was in agreement with the reported value[5].

2-(5-Methoxythiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (14-B). [CAS：596819-12-4]



Method A was used. R_f 0.14 (Hexane/EtOAc = 40/1). Colorless oil (109 mg, 91%).

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.09 (s, 12H), 3.24 (s, 3H), 6.07 (d, *J* = 4.0 Hz, 1H), 7.62 (d, *J* = 3.9 Hz, 1H).

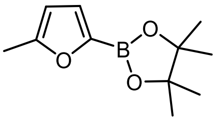
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.32 (s, 12H), 3.92 (s, 3H), 6.30 (d, *J* = 3.8 Hz, 1H), 7.33 (d, *J* = 3.8 Hz, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.9, 59.7, 83.8, 106.4, 137.2, 173.5.

HRMS (EI): Calcd for $C_{16}H_{26}B_2O_4S$ 240.0991, Found 240.0994.

^{1}H NMR spectroscopic data was in agreement with the reported value[5].

4,4,5,5-Tetramethyl-2-(5-methylfuran-2-yl)-1,3,2-dioxaborolane (15-B). [CAS：338998-93-9]



Method A was used. R_f 0.028 (Hexane/EtOAc = 40/1). Colorless oil (71 mg, 68%).

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.09 (s, 12H), 1.99 (s, 3H), 5.81 (d, *J* = 2.3 Hz, 1H), 7.22 (d, *J* = 3.2 Hz, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 13.6, 24.8, 83.7, 107.2, 125.4, 157.6.

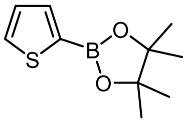
HRMS (EI): Calcd for $C_{11}H_{17}BO_3$ 208.1271, Found 208.1270.

^{1}H NMR spectroscopic data was in agreement with the reported value.[14]

4,4,5,5-Tetramethyl-2-(thiophen-2-yl)-1,3,2-dioxaborolane
and 2,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene.

Method A was used. The product was obtained as a mixture of mono and diborylated thiophenes. It was possible to purify two products by flush column chromatography over silica gel.

4,4,5,5-Tetramethyl-2-(thiophen-2-yl)-1,3,2-dioxaborolane (16-B). [CAS: 193978-23-3]



R_f 0.22 (Hexane/EtOAc = 40/1). White solid (41 mg, 39%).

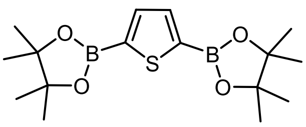
^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.08 (s, 12H), 6.89 (m, 1H), 7.18 (dd, *J* = 0.92, 4.6 Hz, 1H), 7.88-7.89 (m, 1H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.8, 84.0, 128.5, 132.8, 137.7.

HRMS (EI): Calcd for $C_{10}H_{15}BO_2S$ 210.0886, Found 210.0889.

^{1}H NMR spectroscopic data was in agreement with the reported value.[15]

2,5-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)thiophene (16-2B). [CAS: 175361-81-6]



R_f 0.14 (Hexane/EtOAc = 40/1). White solid (54 mg, 32%).

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.03 (s, 24H), 7.97 (s. 2H) .

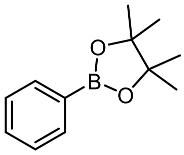
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.34 (s, 24H), 7.66 (s, 2H).

^{13}C NMR (C_6D_6, 100.53 MHz): δ 24.8, 84.1, 138.6.

HRMS (EI): Calcd for $C_{16}H_{26}B_2O_4S$ 336.1738, Found 336.1738.

^{1}H NMR spectroscopic data was in agreement with the reported value.[16]

4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaborolane (17-B). [CAS: 24388-23-6]



Method B was used. R_f 0.20 (Hexane/EtOAc = 40/1). White solid (49 mg, 48%).

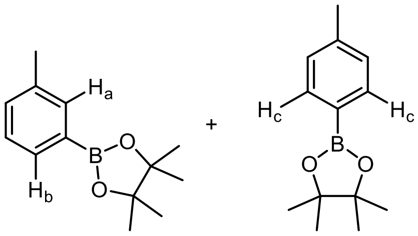
^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.11 (s, 12H), 7.21-7.22 (m, 3H), 8.15-8.17 (m, 2H).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.35 (s, 12H), 7.34-7.38 (m, 2H), 7.44-7.48 (m, 1H), 7.78-7.82 (m, 1H).

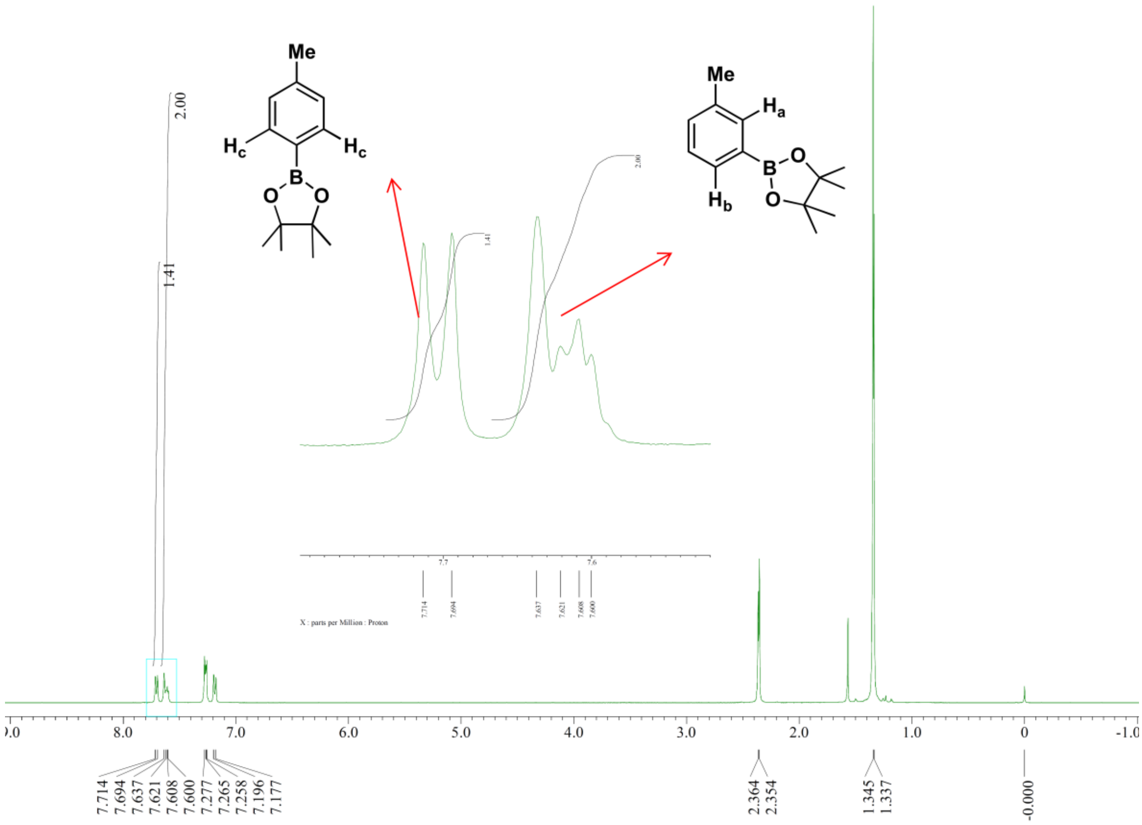
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 25.0, 83.9, 127.8, 131.4, 134.9.

HRMS (EI): Calcd for $C_{12}H_{17}BO_2$ 204.1322, Found 204.1321.

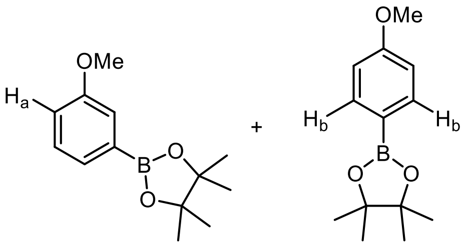
Borylation of toluene (18-B, Table 3).



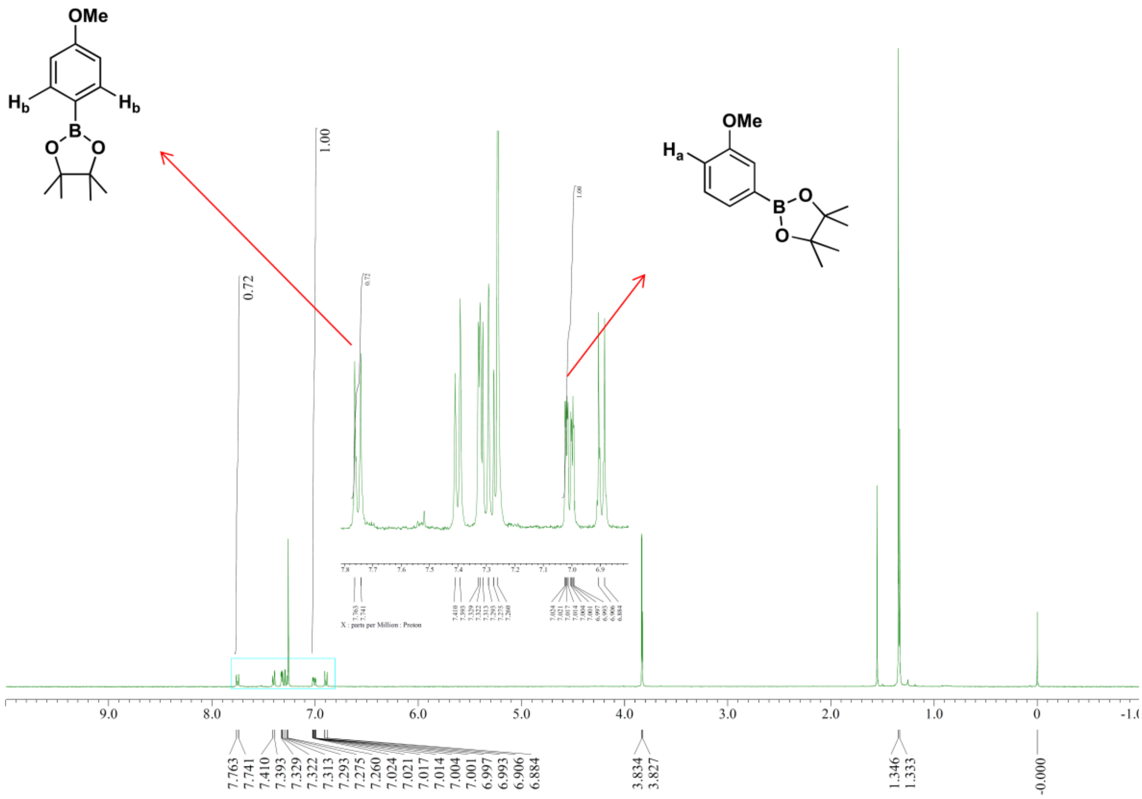
Method B was followed except that the reaction was conducted in toluene (1.0 mL). After purification by flash column chromatography over silica gel eluting with hexane/AcOEt = 20/1, a mixture of two isomers was obtained. GC/MS analysis revealed the two isomers of the borylated products, all of which had an m/z of 218 (M^+). The identity and ratio of each of the two isomers was determined by comparing the ^{1}HNMR spectrum of the product mixture with those reported in the literature.[2a] The resonances specific to each isomer are as follows: ^{1}H NMR ($CDCl_3$, 399.78 MHz): 7.60-7.64 ppm (m, 2H, *meta* isomer , H_a and H_b), 7.70 ppm (d, J = 7.8 Hz, 2H, *para* isomer, H_c).



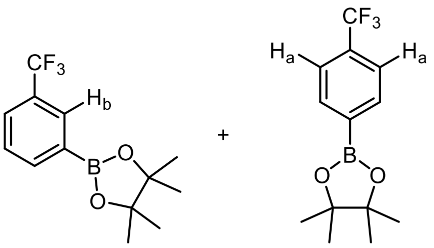
Borylation of anisole (19-B, Table 3).



Method B was followed except that the reaction was conducted in anisole (1.0 mL). After purification by flash column chromatography over silica gel eluting with hexane/AcOEt = 20/1, a mixture of two isomers was obtained. GC/MS analysis revealed the two isomers of the borylated products, all of which had an m/z of 232 (M^+). The identity and ratio of each of the two isomers was determined by comparing the ^{1}HNMR spectrum of the product mixture with those reported in the literature.[2a] The resonances specific to each isomer are as follows: ^{1}H NMR ($CDCl_3$, 399.78 MHz): 7.01 ppm (ddd, J = 0.8, 2.8, 8.0 Hz, 1H, *meta* isomer, H_a), 7.75 ppm (d, J = 8.2 Hz, 2H, *para* isomer, H_b).

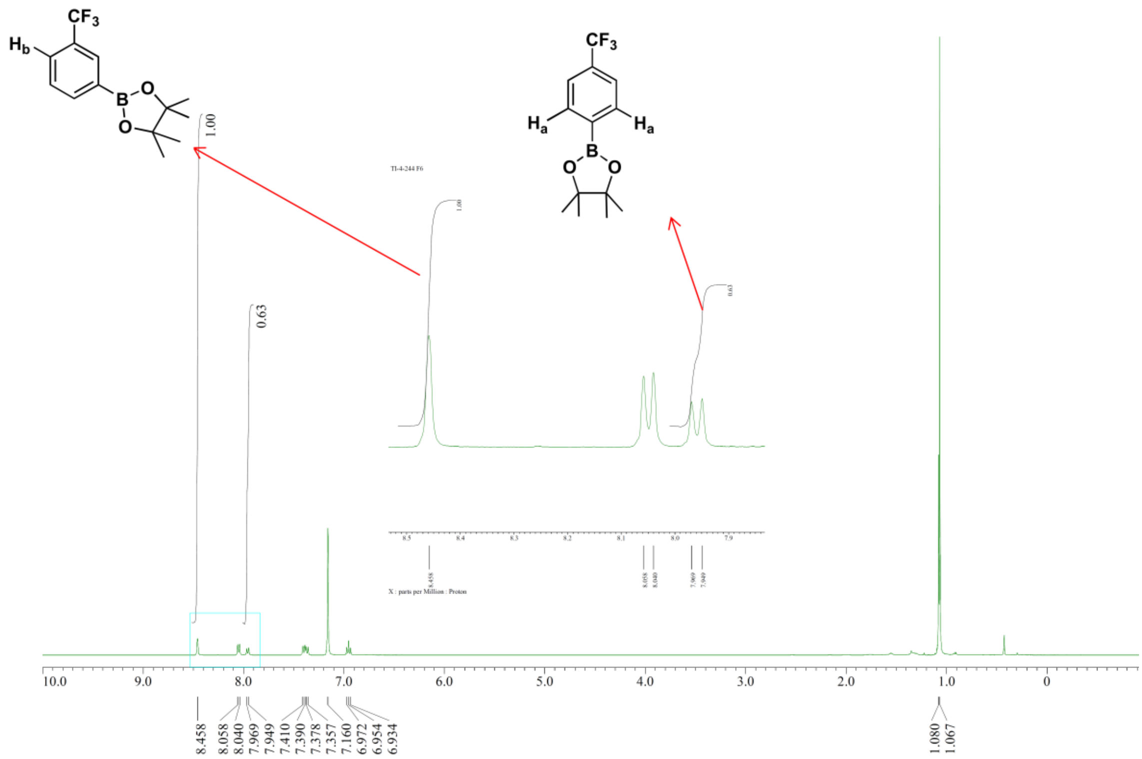


Borylation of trifuluoromethylbenzene (20-B, Table 3).

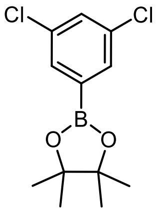


37% 12%

Method B was followed except that the reaction was conducted in trifluoromethylbenzene (1.0 mL). After purification by flash column chromatography over silica gel eluting with hexane/AcOEt = 40/1, a mixture of two isomers was obtained. GC/MS analysis revealed the two isomers of the borylated products, all of which had an m/z of 272 (M^+). The identity and ratio of each of the two isomers was determined by comparing the ^{1}HNMR spectrum of the product mixture with those reported in the literature.[2a] The resonances specific to each isomer are as follows: ^{1}H NMR (C_6D_6, 399.78 MHz): 7.96 (d, J = 8.2 Hz, 1H, *para* isomer, H_a), 8.46 (s, 1H, *meta* isomer, H_b).



2-(3,5-Dichlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (21-B). [CAS: 68716-51-8]



Method B was followed except that the reaction was conducted in 1,3-dichlorobenzene (1.0 mL).

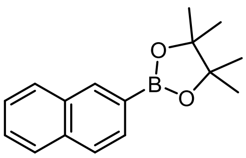
White solid (42 mg, 31%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.34 (s, 12H), 7.43 (t, J = 2.2 Hz, 1H), 7.64 (d, J = 2.3 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 25.0, 84.7, 131.2, 132.9, 134.9.

HRMS (EI): Calcd for $C_{12}H_{15}BCl_2O_2$ 272.0542, Found 272.0540.

4,4,5,5-Tetramethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborolane (22-B). [CAS：256652-04-7]



In a glovebox, $[Ir(cod)(OMe)]_2$ (33.1 mg, 0.050 mmol, 0.10 equiv), ICy•HCl (26.2 mg, 0.10 mmol, 0.20 equiv), NaO^{t}Bu (19.2 mg, 0.20 mmol, 0.40 equiv) and methylcyclohexane (1.0 mL) were added to a 10 mL-sample vial with Teflon-sealed screwcap, and stirred for 5 min at room temperature. A naphthalene (384.1 mg, 3.0 mmol, 6.0 equiv) and **1** (113.1 mg, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 110 °C for 4 h. After the reaction mixture was cooled to room temperature, the pinacol (236 mg, 2.0 mmol) in THF (2.0 mL) was added and stirred for 1.5 h at room temperature under N_2. The crude mixture was filtered through a pad of Celite eluting with AcOEt. The filtrate was concentrated in vacuo and analyzed by ^{1}HNMR using 1,2-dichloroethane as an internal standard. The crude mixture was concentrated under reduced pressure again, and purified by flash column chromatography over silica gel eluting with Hexane/AcOEt (40/1) solution. The filtrate was concentrated in vacuo to give a pure borylated product as a white solid (63.5 mg, 50%).

R_f 0.17 (Hexane/EtOAc = 40/1). White solid (64 mg, 50%).

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.16 (s, 12H), 7.19-7.24 (m, 2H), 7.6 (d, *J* = 8.2 Hz, 1H), 7.69 (t, *J* = 18.3, 18.3 Hz, 2H), 8.23 (d, *J* = 7.3 Hz, 1H), 8.75 (s, 1H).

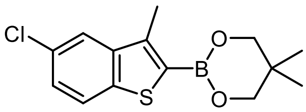
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.40 (s, 12H), 7.47-7.53 (m, 2H), 7.82-7.83 (m, 3H), 7.89 (d, *J* = 7.8 Hz, 1H), 8.37 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 25.0, 84.0, 125.9, 127.0, 127.8, 128.7, 130.5, 132.9, 135.1, 136.3. One carbon peak is overlapped with solvent peaks.

HRMS (EI): Calcd for $C_{16}H_{19}BO_2$ 254.1478, Found 254.1482.

^{1}H NMR spectroscopic data was in agreement with the reported value.[17]

2-(5-Chloro-3-methylbenzo[*b*]thiophen-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (10-Bnep).



Method A was followed except that after the reaction mixture was cooled to room temperature, the neopentyl glycol (208 mg, 2.0 mmol) in THF (2.0 mL) was added and stirred for 1.5 h at room temperature under N_2.

R_f 0.085 (Hexane/EtOAc = 40/1). White Solid (130 mg, 88%). Mp = 119 °C.

^{1}H NMR (C_6D_6, 399.78 MHz): δ 0.53 (s, 6H), 2.50 (s, 3H), 3.32 (s, 4H), 7.08 (dd, *J* = 1.8, 7.8 Hz, 1H), 7.27 (d, *J* = 7.3 Hz, 1H), 7.69 (d, *J* = 2.3 Hz, 1H).

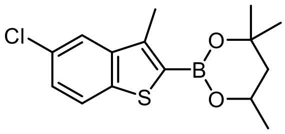
^{13}C NMR (C_6D_6, 100.53 MHz): δ 13.7, 21.5, 31.5, 72.2, 122.6, 124.0, 125.7, 130.3, 141.4, 141.6, 143.5.

IR (ATR): 2964 w, 2936 w, 1895 w, 1580 w, 1555 w, 1525 m, 1475 w, 1438 w, 1415 m, 1375 w, 1341 m, 1290 s, 1272 s, 1244 s, 1149 w, 1117 s, 1074 m, 1028 w, 977 w, 933 w, 916 w, 894 w, 865 w, 850 m, 809 s, 729 w, 697 w, 669 m.

MS m/z (% relative intensity) : 296 (38), 295 (27), 294 (M^+, 100), 293 (30), 260 (12), 259 (67), 258 (21), 208 (15), 207 (14), 181 (14), 173 (15).

HRMS (EI): Calcd for $C_{14}H_{16}BClO_2S$ 294.0653, Found 294.0653.

2-(5-Chloro-3-methylbenzo[*b*]thiophen-2-yl)-4,4,6-trimethyl-1,3,2-dioxaborinane (10-Bmep).



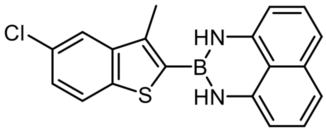
Method A was followed except that after the reaction mixture was cooled to room temperature, the 2-methylpentane-2,4-diol (236 mg, 2.0 mmol) in THF (2.0 mL) was added and stirred for 1.5 h at room temperature under N_2.

R_f 0.23 (Hexane/EtOAc = 40/1). Colorless oil (134 mg, 87%).

^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.00 (s, 3H), 1.06 (d, *J* = 6.4 Hz, 3H), 1.12-1.14 (m, 5H), 2.57 (s, 3H), 3.87-3.95

(m, 1H), 7.08 (dd, J = 1.8, 8.5 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 1.8 Hz, 1H).
^{13}C NMR (C_6D_6, 100.53 MHz): δ 13.6, 23.0, 28.0, 31.1, 45.7, 65.5, 71.7, 122.5, 123.9, 125.6, 130.3, 141.1, 141.3, 143.5.
IR (ATR): 2973 w, 2914 w, 2360 w, 2340 w, 1737 w, 1581 w, 1554 w, 1523 w, 1440 w, 1396 m, 1379 w, 1344 m, 1319 w, 1286 s, 1265 s, 1243 s, 1206 m, 1160 m, 1109 m, 1077 m, 1059 w, 1027 w, 980 w, 963 w, 937 w, 901 w, 864 w, 851 w, 823 w, 799 m, 768 m, 730 w, 692 w, 972 m.
MS m/z (% relative intensity) : 310 (38), 309 (26), 308 (M^+, 100), 307 (24), 254 (13), 252 (35), 251 (13), 237 (16), 225 (11), 211 (18), 210 (42), 209 (57), 208 (97), 207 (24), 182 (11), 181 (18), 173 (26), 83 (21), 55 (10), 43 (26).
HRMS (EI): Calcd for $C_{15}H_{18}BClO_2S$ 308.0809, Found 308.0804.

2-(5-Chloro-3-methylbenzo[*b*]thiophen-2-yl)-2,3-dihydro-1*H*-naphtho[1,8-*de*][1,3,2]diazaborinine (10-Bdan).



Method A was followed except that after the reaction mixture was cooled to room temperature, the 1,8-naphthalenediamine (316 mg, 2.0 mmol) in THF (2.0 mL) was added and stirred for 1.5 h at room temperature under N_2.
R_f 0.29 (Hexane/EtOAc = 20/1). White solid (131 mg, 75%). Mp = 173 °C.
^{1}H NMR (C_6D_6, 399.78 MHz): δ 1.97 (s, 3H), 5.32 (s, 2H), 5.92 (dd, J = 0.92, 7.3 Hz, 2H), 7.02-7.15 (m, 5H), 7.33 (d, J = 8.2 Hz, 1H). 7.65 (d, J = 1.8 Hz, 1H).
^{13}C NMR (C_6D_6, 100.53 MHz): δ 13.9, 106.8, 118.8, 120.6, 122.2, 123.8, 125.5, 130.9, 136.9, 137.0, 140.3, 140.8, 143.0.
IR (ATR): 3428 w, 3415 w, 3049 w, 2360 w, 1734 w, 1627 w, 1596 s, 1554 w, 1528 m, 1497 m, 1437 w, 1405 m, 1371 m, 1337 m, 1281 w, 1195 m, 1164 m, 1099 m, 1074 m, 1035 w, 935 w, 859 m, 814 m, 798 m, 751 s, 660 s.
MS m/z (% relative intensity): 350 (42), 349 (32), 348 (M^+, 100), 347 (29), 174 (15), 173 (14), 166 (38), 165 (21).
HRMS (EI): Calcd for $C_{19}H_{14}BClN_2S$348.0659, Found 348.0662.

1.5 References

(1) A review on the catalytic borylation of aromatic C-H bonds: Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890.

(2) (a) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390. (b) Ishiyama, T.; Takagi, J.; Hartwig, J. F.; Miyaura, N. *Angew. Chem. Int. Ed.* **2002**, *41*, 3056.

(3) Frey, G. D.; Rentzsch, C. F.; von Preysing, D.; Scherg, T.; Mühlhofer, M.; Herdtweck, E.; Herrmann, W. A. *J. Organomet. Chem.* **2006**, *691*, 5725.

(4) (a) Obligacion, J. V.; Semproni, S. P.; Chirik, P. J. *J. Am. Chem. Soc.* **2014**, *136*, 4133. (b) Furukawa, T.; Tobisu, M.; Chatani, N. *Chem. Commun.* **2015**, *51*, 6508. (c) Zhang, H.; Hagihara, S.; Itami, K. *Chem. Lett.* **2015**, *44*, 779. (d) Furukawa, T.; Tobisu, M.; Chatani, N. *J. Am .Chem. Soc.* **2015**, *137*, 12211.

(5) Our group has developed catalytic reactions using ICy as the best ligand: (a) Tobisu, M.; Yasutome, A.;

Kinuta, H.; Nakamura, K.; Chatani, N. *Org. Lett.* **2014**, *16*, 5572. (b) Tobisu, M.; Takahira, T.; Ohtsuki, A.; Chatani, N. *Org. Lett.* **2015**, *17*, 680. (c) Tobisu, M.; Takahira, T.; Chatani, N. *Org. Lett.* **2015**, *17*, 4352. (d) Tobisu, M.; Morioka, T.; Ohtsuki, A.; Chatani, N. *Chem. Sci.* **2015**, *6*, 3410. (e) Morioka, T.; Nishizawa, A.; Nakamura, K.; Tobisu, M.; Chatani, N. *Chem. Lett.* **2015**, *44*, 1729. (f) Nakamura, K.; Tobisu, M.; Chatani, N. *Org. Lett.* **2015**, *17*, 6142. (g) Furukawa, T.; Tobisu, M.; Chatani, N. *Bull. Chem. Soc. Jpn.* **2017**, *90*, 332. (h) Ohtsuki, A.; Sakurai, S.; Tobisu, M.; Chatani, N. *Chem. Lett.* **2016**, *45*, 1277. see also (4b) and (4d).

(6) (a) Ishiyama, T.; Ishida, K.; Takagi, J.; Miyaura, N. *Chem. Lett.* **2001**, *30*, 1082. (b) Cho, S. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 8157. (c) Larsen, M. A.; Wilson, C. V.; Hartwig, J. F. *J. Am. Chem. Soc.* **2015**, *137*, 8633. (d) Palmer, W. N.; Obligacion, J. V.; Pappas, I.; Chirik, P. J. *J. Am. Chem. Soc.* **2016**, *138*, 766. (e) Palmer, W. N.; Zarate, C.; Chirik, P. J. *J. Am. Chem. Soc.* **2017**, *139*, 2589. (f) Kelley, C. M.; Fuller III, J. T.; Macaulay, C. M.; Mcdonald, R.; Ferguson, M. J.; Bischof, S. M.; Sydora, O. L.; Ess, D. H.; Stradiotto, M.; Turculet, L. *Angew. Chem. Int. Ed*. **2017**, *56*, 6312. see also (4b).

(7) The catalytic borylation of aromatic C-H bonds using $B_2(nep)_2$ or $B_2(hg)_2$: Liskey, C. W.; Hartwig, J. F. *Synthesis* **2013**, *45*, 1837.

(8) The catalytic borylation of aromatic C-H bonds using HBdan: Iwadate, N.; Suginome, M. *J. Organomet. Chem.* **2009**, *694*, 1713.

(9) Noguchi, H.; Hojo, K.; Suginome, M. *J. Am. Chem. Soc.* **2007**, *129*, 758.

(10) Nickel-catalyzed borylation of aromatic C-H bonds: Zhang, H.; Hagihara, S.; Itami, K. *Chem. Lett.* **2015**, *44*, 779. see also (4b).

(11) Greulich, T. W.; Daniliuc, C. G.; Studer, A. *Org. Lett.* **2015**, *17*, 254.

(12) (a) Marciasini, L.; Richy, N.; Vaultier, M.; Pucheault, M. *Chem. Commun.* **2012**, *448*, 1553. (b) Marciasini, L.; Richy, N.; Vaultier, M.; Pucheault, M. *Adv. Synth. Catal.* **2013**, *6*, 1083.

(13) Stadlwieser, J. F.; Dambaur, M. E. *Helv. Chim. Acta.* **2006**, *89*, 936.

(14) Hatanaka, T.; Ohki, Y.; Tatsumi, K. *Chem. Asian. J.* **2010**, *5*, 1657.

(15) Boller, T. M.; Murphy, J. M.; Hapke, M.; Ishiyama, T.; Miyaura, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 14263.

(16) Guerrand, H. D. S.; Marciasini, L. D.; Jousseaume, M.; Vaultier. M.; Pucheault, M. *Chem. Eur. J.* **2014**, *20*, 5573.

(17) Kinuta, H.; Tobisu, M.; Chatani, N. *J. Am. Chem. Soc.* **2015**, *137*, 1593.

Chapter 2

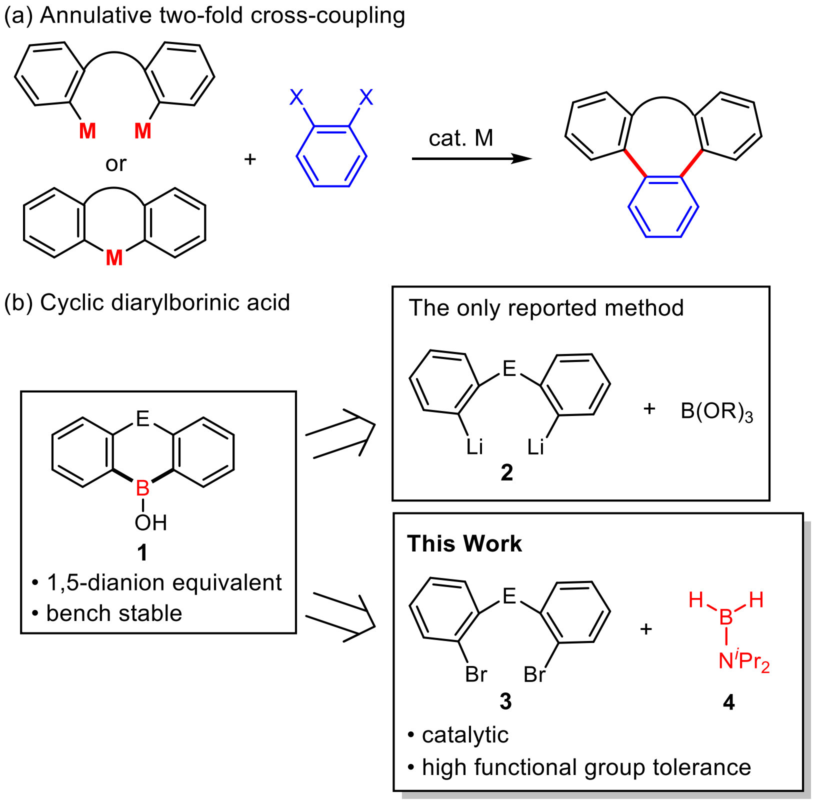
Palladium-Catalyzed Two-Fold Borylation Using Diisopropylaminoborane for the Synthesis of Cyclic Diarylborinic Acids

2.1 Introduction

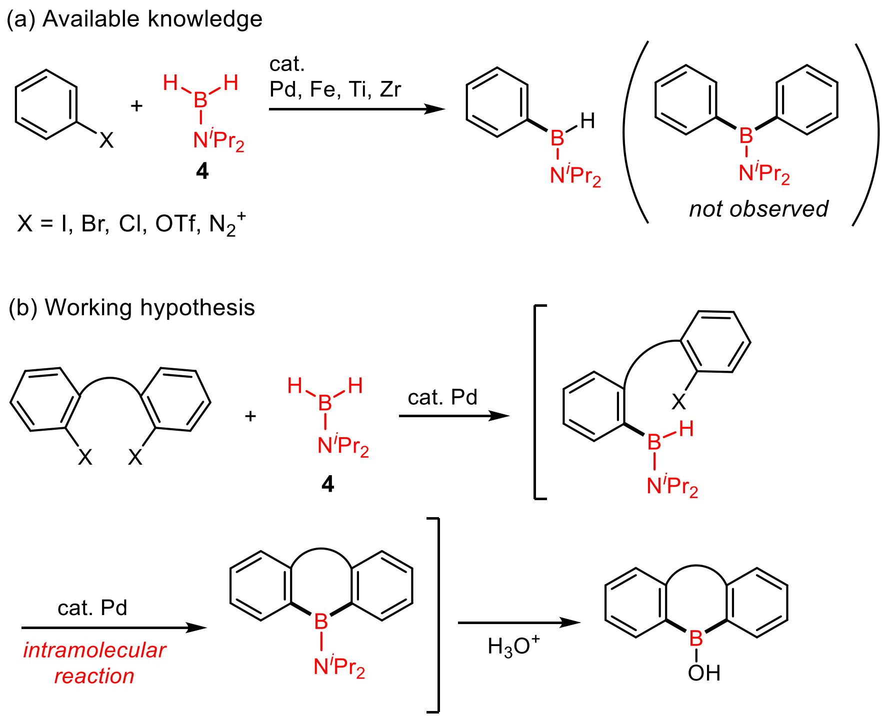
The development of synthetic methods for π-conjugated molecules is essential for the creation of new functional organic materials, such as light emitting diodes, transistors and solar cells.[1] The annulative two-fold $C(sp^2)$-$C(sp^2)$ cross-coupling reactions between organodimetallic reagents and dilalides is one of the powerful methods for this purpose (**Scheme 1a**). Among the reported organodimetallic reagents,[2] cyclic diarylborinic acids **1**[3] are useful, because of its low toxicity and stability towards air and moisture. However, the potential utility of **1** has been limited, because all of the reported synthetic methods for **1** require the use of organolithium reagents **2**.[3] This makes it impossible to synthesize **1** bearing various functional groups (**Scheme 1b**).

Herein, the Pd-catalyzed annulative two-fold $C(sp^2)$-$C(sp^2)$ cross-coupling reactions between dilalides **3** and diisopropylaminoborane **4** was investigated (**Scheme 1b**). However, although many catalytic borylation reactions of aryl halides with **4** have been reported, no reaction using both of two B-H bonds in **4** have been reported even in the presence of an excess amount of the aryl halides (**Scheme 2a**).[4] This suggests that the second B-H bond of **4** has the low reactivity. Nevertheless, it was expected that the second borylation would be facilitated in my intramolecular system (**Scheme 2b**).

Scheme 1. Cyclic Diarylborinic Acids **1** and Methods for its Preparation



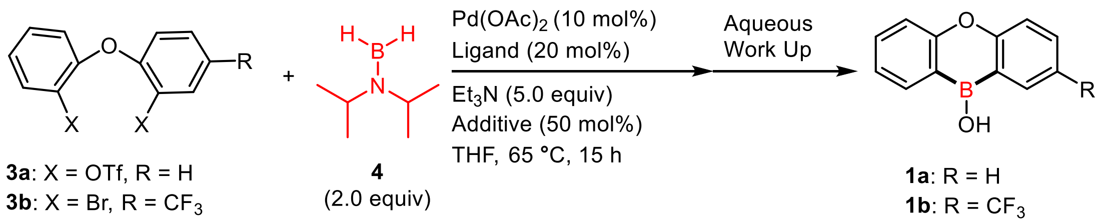
Scheme 2. Working Hypothesis



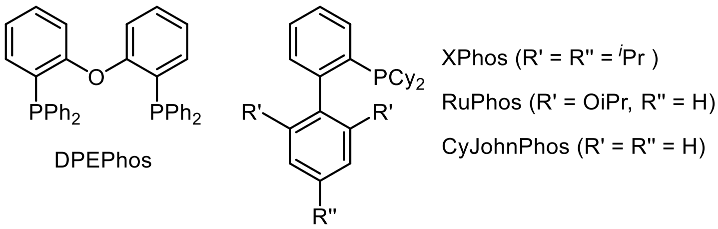
2.2 Results and Discussion

To test the hypothesis (**Scheme 2b**), the author initially examined the reaction of ditriflate **3a** with **4** (2.0 equiv) in the presence of a Pd catalyst at 65 °C for 15 h (**Table 1**). The yield of borylated product **1a** was estimated by ^{1}H NMR spectroscopy after the treatment with methanol and an aqueous solution of NH_4Cl. A brief screening of the ligands revealed that a bisphosphine with a diphenyl ether backbone (i.e., DPEPhos) displayed the highest activity, giving the cyclic boron **1a** in >99% NMR yield (Entry 1). The product **1a** could be isolated in 76% yield by column chromatography. Unfortunately, however, reactions under these optimized conditions using DPEPhos failed to promote the borylation of dibromide **3b** (Entry 2). Biarylphosphine ligand, XPhos afforded product **1b** in 6% yield (Entry 3). Furthermore, the addition of KI greatly improved the yield (Entry 4).[4f] As the results of examining several biaryl phosphine ligands in the presence of KI, the simplest CyJohnPhos[5] was found to be the best ligand to form **1b** in 97% yield (Entry 6).

Table 1. Optimization of the Reaction Conditions



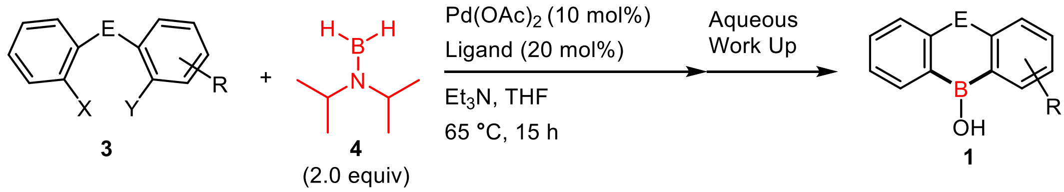
Entry	Substrate	Ligand	Additive	NMR yield
1	**3a**	DPEPhos	none	>99 (76)[b]
2	**3b**	DPEPhos	none	0
3	**3b**	XPhos	none	6
4	**3b**	XPhos	KI	68
5	**3b**	RuPhos	KI	60
6	**3b**	CyJohnPhos	KI	97 (75)[b]

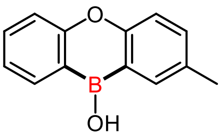


[a] Reaction conditions: **3a** or **3b** (0.50 mmol), **4** (1.0 mmol), $Pd(OAc)_2$ (0.050 mmol), ligand (0.10 mmol), Et_3N (2.5 mmol), additive (0.25 mmol) in THF (2 mL) at 65 °C for 15 h. [b] Isolated yields are shown.

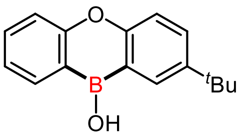
The reaction was successfully applied to the synthesis of a series of cyclic diarylborinic acids (**Table 2**). In addition to diarylborinic acids bearing simple alkyl, aryl and alkoxy groups (**1c-1h**), those containing cyano, chloro, ester, amide, carbamate and fluoro groups (**1i-1o**) were all compatible with these catalytic conditions. This highlights the synthetic advantage of my protocol over previously reported methods using organolithium reagents.[3] In particular, the tolerance of an aryl chloride moiety, as shown for **1k**, is notable when considering the report that the borylation of aryl chlorides with **4** occurs using a Pd/XPhos catalyst.[4f] My protocol also allowed the synthesis of π-extended analogue **1p** as well as diarylborinic acids containing nitrogen (**1q**) and sulfur (**1r**) tethers. Notably, seven-membered diarylborinic acid **1s** was successfully synthesized.[6] Although the author routinely isolated the product after hydrolysis in the form of borinic acid **1**, column chromatographic separation led to a considerable loss of **1** in some cases (numbers in parentheses in **Table 2** refer to isolated yields). However, this issue could be easily addressed by the formation of an aminoalcohol adduct, such as **1j**,[7] which could be isolated by simple filtration and used directly for the subsequent two-fold cross-coupling (vide infra).

Table 2. Scope of the Substrates[a]

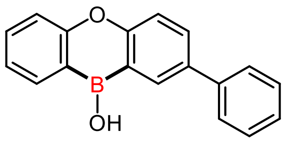




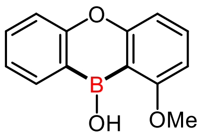
1c 91% (74%)
X = Y = OTf



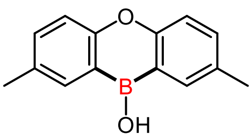
1d 88% (68%)
X = Y = OTf



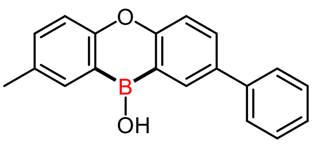
1e 80% (58%)
X = Y = OTf



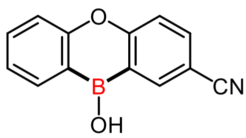
1f 58% (43%)
X = Y = OTf



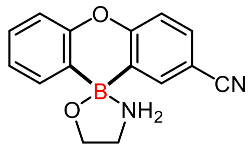
1g >99% (75%)
X = Y = OTf



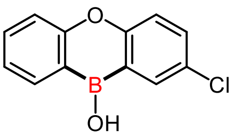
1h >99% (70%)
X = Y = OTf



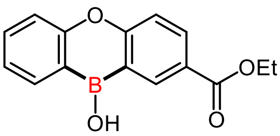
1i 96% (72%)
X = Y = Br[b]



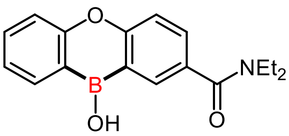
1j (85%)
X = Y = Br[b,c]



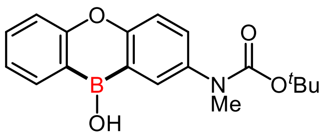
1k >99% (77%)
X = I, Y = Br[b]



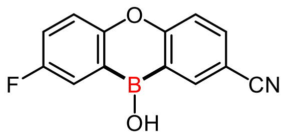
1l 98% (81%)
X = Y = Br[b]



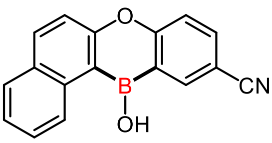
1m 78% (65%)
X = Y = Br[b]



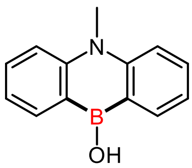
1n >99% (72%)
X = Y = Br[b]



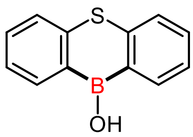
1o 54% (23%)
X = Y = Br[b]



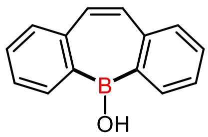
1p 45% (26%)
X = Y = Br[b]



1q 56% (42%)
X = Y = Br[b]



1r 71% (55%)
X = Y = Br[b]

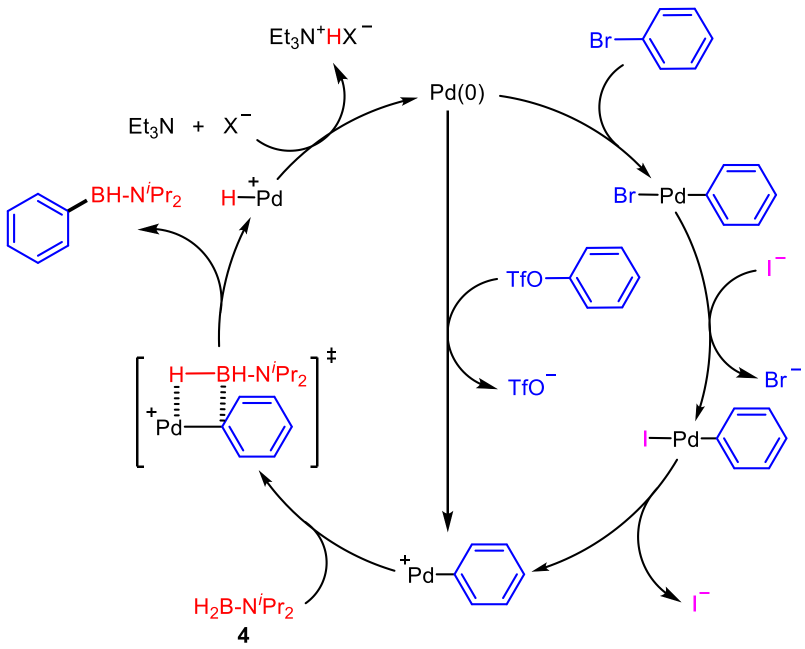


1s 68% (37%)[d]
X = Y = Br[b]

[a] Reaction conditions: **3** (0.50 mmol), **4** (1.0 mmol), $Pd(OAc)_2$ (0.050 mmol), ligand (0.10 mmol), Et_3N (2.5 mmol) in THF (2 mL) at 65 °C for 15 h. Ligand: DPEPhos for ditriflates **3c-3h**; CyJohnPhos for dibromides **3i-3o** and **3s**; XPhos for **3p** and **3r**; RuPhos for **3q**. ^{1}H-NMR yields are shown. Numbers in parentheses are isolated yields. [b] KI was added. [c] After the reaction, 2-aminoethanol (4.0 equiv) was added. [d] Using 1.0 g of **3s**.

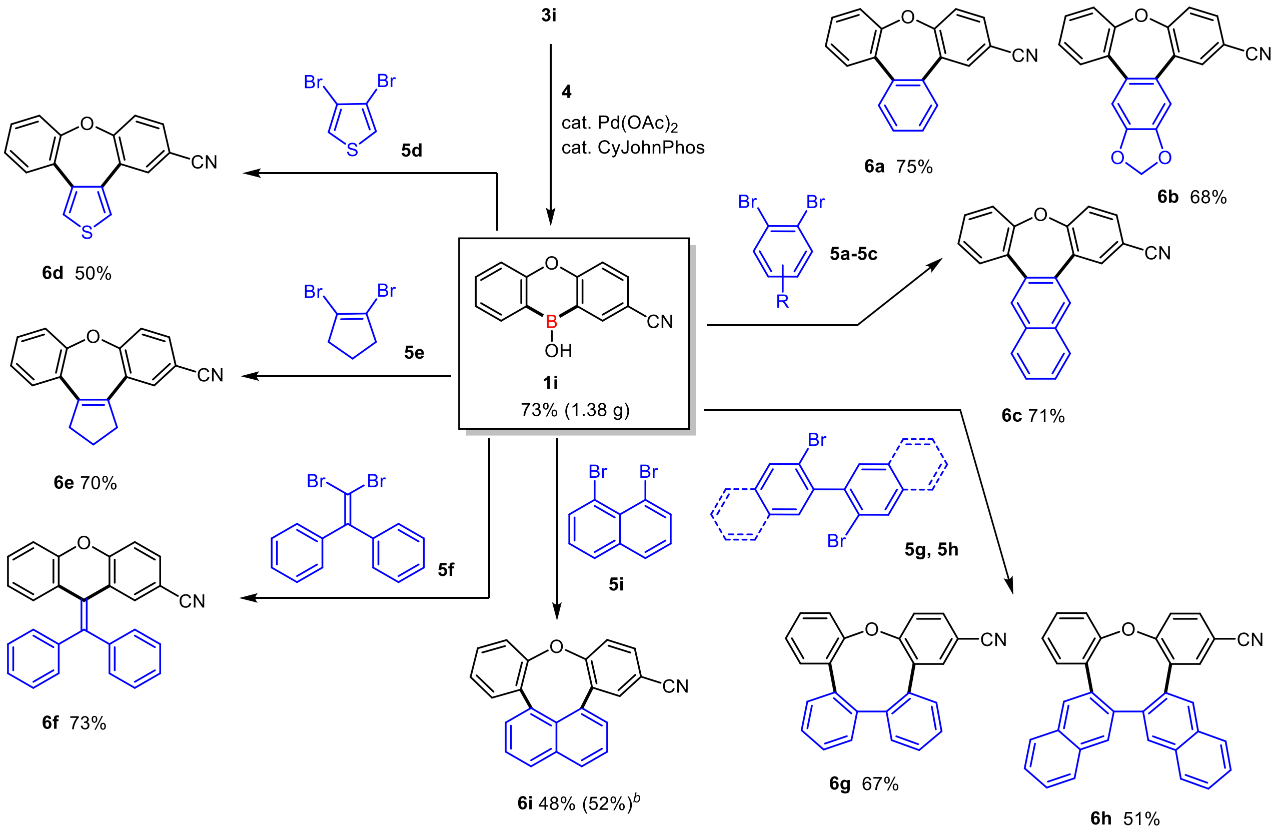
As the author have seen so far, the addition of KI is essential for an efficient reaction, when dibromides were used as substrates (**Table 1, 2**). In contrast, the cyclization proceeded effectively even in the absence of KI when using ditriflate. A possible mechanism is shown in **Scheme 3**, when considering the effect of KI. Marder and Lin reported on a mechanism for the Pd-catalyzed borylation of aromatic halides with **4** using DFT calculations.[8] The initial step involves oxidative addition of phenyl boromide to Pd(0) to form the phenylpalladium bromide intermediate. The direct reaction of this phenyl palladium bromide with **4** is energetically unfavorable. Instead, the reaction with **4** is more favored from the cationic phenyl palladium species. The dissociation of the halide ligand needs to occur for an efficient transmetallation. Based on this proposal, it is believed that the role of KI is to convert arylpalladium boromide to the corresponding iodide. This iodide is much easier to generate a cationic palladium species. This cationic phenyl palladium rapidly reacts with **4** to form the desired borylated product. This mechanistic proposal also explains why KI is not required for the reaction of aromatic triflate. Because triflate is a better leaving group than bromide, a cationic palladium is easily generated without the aid of KI. In this catalytic synthesis of cyclic diarylborinic acids, this borylation takes place twice.

Scheme 3. Plausible Mechanism



My catalytic protocol can be readily performed to the gram scale synthesis of cyclic diarylborinic acids (**Scheme 4**, **3i**→**1i**). The obtained functionalized boracycle can then serve as a 1,5-dianion equivalent in annulative two-fold cross-coupling with dihalides under a Pd catalysis, and thus allows access to a diverse range of π-extended heteroarenes (**Scheme 4**).[3e] For example, cross-coupling of **1i** with 1,2-dibromo(hetero)arenes **5a-5d** enabled the efficient synthesis of the tribenzo[*b*,*d*,*f*]oxepine skeleton in **6a-6c** or the heteroarene-fused analogue **6d**. This structural motif is found in antidepressant drugs[9] and natural products.[10] In addition, cross-coupling of **1i** with 1,2-dibromocyclopentene **5e** proceeded efficiently to afford corresponding dibenzo[*b*,*f*]oxepin derivative **6e**. π-Extended xanthene derivative **6f** was also assembled by cross-coupling of **1i** with 1,1-dibromoalkene **5f**, valuable finding with respect to potential application in the synthesis of molecular probes for aggregation induced emission.[11] Moreover, a larger ring system can also be accessible by the reaction of **1i** with dibromobiaryl **5g** and **5h**, which led to the formation of a tetrabenzo[*b*,*d*,*f*,*h*]oxonine skeleton **6g** and **6h**.[12] Cross-coupling with 1,8-dibromonaphthalene **5i** affored dibenzo[*b*,*g*]naphtho[1,8-*de*]oxocine framework **6i**, for which a synthetic method has not previously been reported. This modular assembly of six- to nine-membered π systems by simply changing the dihalide coupling partners highlights the synthetic utility of the cyclic diarylborinic acids.

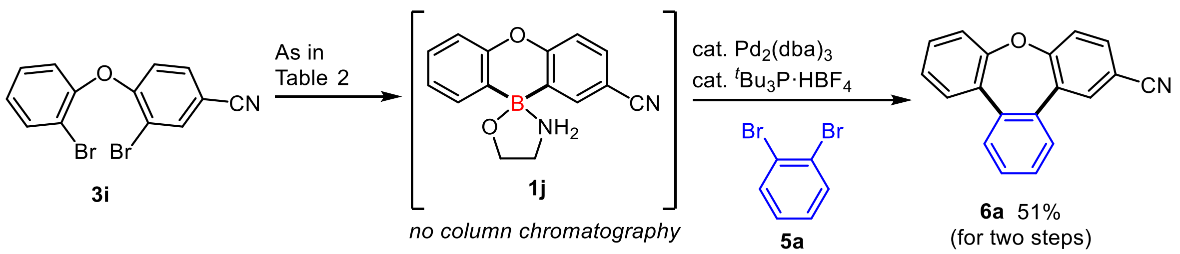
Scheme 4. Scalability for the Synthesis of Cyclic Diarylborinic Acids and Pd-Catalyzed Annulative Two-Fold Suzuki-Miyaura Coupling for the Synthesis of Benzannulated Heterocycles[a]



[a] Reaction conditions: **1i** (0.25 mmol), **5** (0.50 mmol), $Pd_2(dba)_3$ (0.0038 mmol), ${}^tBu_3P{\bullet}HBF_4$ (0.0090 mmol), Cs_2CO_3 (0.83 mmol), H_2O (2.5 mmol) in ^{t}AmOH (3 mL) at 100 °C for 24-48 h. Yields of isolated products are shown. [b] Run on a 1.0 mmol scale.

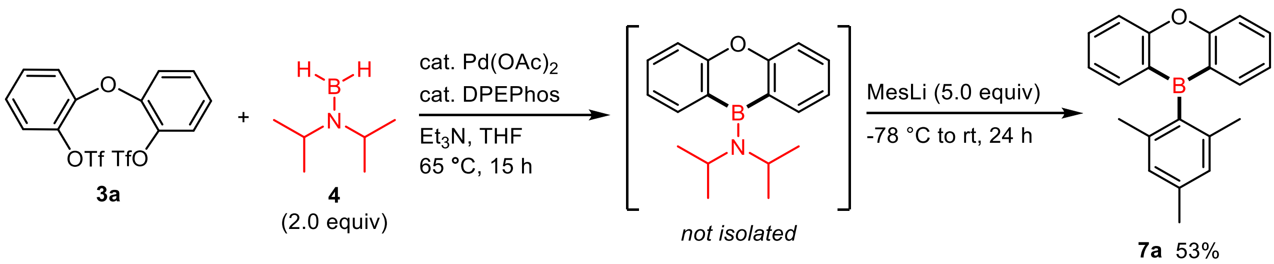
Importantly, this annulative two-fold cross-coupling can be applied directly from dihalide **3** and **4** without the need for column chromatographic isolation of borinic acid **1** (**Scheme 5**). The Pd-catalyzed reaction of **3i** and **4**, followed by the treatment with 2-aminoethanol, led to the formation of borinate **1j**, which could be isolated by simple filtration. This product was used directly in a subsequent annulation with **5a** to give **6a** in 51% overall yield.

Scheme 5. Pd-Catalyzed Two-Fold Suzuki-Miyaura Coupling Using Cyclic Vorinate **1j**



In addition to their use as a 1,5-dianion equivalent, cyclic diarylborinic acid derivatives can also serve as useful precursors to functional organoboron compounds. For example, the annulative reaction of ditriflate **3a** with **4**, followed by addition of MesLi instead of aqueous work up, led to the construction of 9-mesityl-9*H*-boraxanthene **7a**, a class of fluorescent compounds that are currently attracting much attention (**Scheme 6**).[13]

Scheme 6. One-Pot Synthesis of 9-Mesityl-9*H*-boraxanthene **7a**



2.3 Conclusion

In summary, the author has developed the catalytic method for the synthesis of cyclic diarylborinic acids through the two-fold annulative borylation of dihalides using both of two B-H bonds in diisopropylaminoborane. This method allows the synthesis of cyclic diarylborinic acids bearing various functional groups, which could not be synthesized by previously reported methods using organolithium reagents. Furthermore, cyclic diarylborinic acids can serve as non-toxic and stable building blocks for the rapid synthesis of π-conjugated molecules through annulative two-fold Suzuki-Miyaura cross coupling reactions with dihalides. It is expected that the unique compound libraries given by this reaction accelerates the discovery of new functional materials.

2.4 Experimental Section

2.4.1 General Information

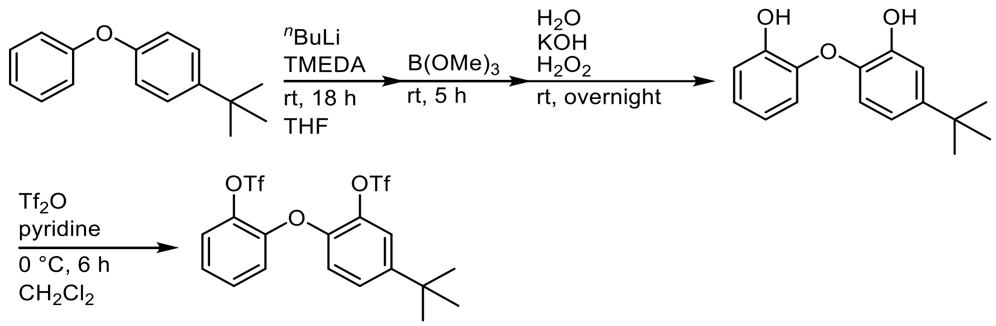
^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL ECS-400 spectrometer in $CDCl_3$ or C_6D_6 with tetrachloroethane as the internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad peak), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained using a JASCO FT/IR-4200 spectrometer; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra and high resolution mass spectra (HRMS) were obtained on a JEOL JMS-700 spectrometer. Analytical gas chromatography (GC) was carried out on a Shimazu GC-2014 gas chromatograph, equipped with a flame ionization detector. Melting points were determined using a Yamato melting point apparatus. UV vis absorption spectrum was obtained on a Shimazu UV-1800 UV spectrophotometer. Column chromatography was performed with SiO_2 (silicycle SilicaFlash F60 (230-400 mesh)).

2.4.2 Materials

$Pd(OAc)_2$ (Wako), DPEPhos (Wako), Xantphos (Wako), 2-(dicyclohexylphosphino)-biphenyl (TCI), 2-dicyclohexylphosphino-2’,4’,6’-triisopropylbiphenyl (Aldrich), dicyclohexyl(2’,6’-diisopropoxy-[1,1’-biphenyl]-2-yl)phosphine (Wako), Et_3N (Nacalai tesque), KI (Wako), THF (super dehydrated, TCI), MeOH (super dehydrated, Wako), NH_4Cl (Nacalai tesque), $MgSO_4$ anhydrous (Nacalai tesque), $NaSO_4$ (anhydrous, Nacalai tesque), 2-aminoethanol (TCI), Pd_2dba_3 (Aldrich), $^tBu_3PH(BF_4)$ (TCI), ^{t}AmOH (TCI), **5a** (TCI), **5b** (TCI), **5c** (TCI), **5d** (TCI), **5e** (Wako), **5g** (TCI), **5h** (TCI) and **5i** (TCI) were purchased from the commercial suppliers, and used as received.

3q [CAS: 87345-09-3],[14] **3r** [CAS: 21848-84-0],[15] **3s** [CAS: 56667-11-9],[16] **4** [CAS: 22092-92-8],[17] and **5f** [CAS: 2592-73-6][18] were prepared according to the literature methods.

2-(4-(*tert* -Butyl)-2-(((trifluoromethyl)sulfonyl)oxy)phenoxy)phenyl trifluoromethanesulfonate (3d).



^{n}BuLi (1.6 M in hexane, 21 mL, 33 mmol, 2.2 equiv) was slowly added to a solution of 1-(*t*-butyl)-4-phenoxybenzene[19] (3.4 g, 15 mmol, 1.0 equiv) in THF (15 mL) at room temperature. After the addition of *N,N,N’,N’*-tetramethylethylenediamine (TMEDA, 5.0 mL, 33 mmol, 2.2 equiv), the mixture was stirred for 18 h at room temperature. $B(OMe)_3$ (6.7 mL, 59 mmol, 4.0 equiv) was added and the mixture was stirred for further 5 h. A solution of KOH (2.3 g, 41 mmol, 2.7 equiv) and 30% H_2O_2 (5.7 mL) in H_2O (19 mL) was then added to the mixture, which was further stirred 18 h at room temperature. After the mixture was acidified to pH 1 with 2 M HCl, the mixture was extracted with $CHCl_3$, dried over $MgSO_4$. The solvent was then removed under reduced pressure, and the residue was purified by flash column chromatography over silica gel eluting with hexane/EtOAc solution. The collected fractions were recrystallized from hexane/$CHCl_3$ to give 5-(*t*-butyl)-2-(2-hydroxyphenoxy)phenol as a pale yellow solid (1.4 g, 36%).

5-(*t*-Butyl)-2-(2-hydroxyphenoxy)phenol (1.3 g, 5.0 mmol, 1.0 equiv) was dissolved in a solution of dehydrated pyridine (1.6 mL) in dehydrated CH_2Cl_2. To this solution, Tf_2O (2.9 g, 10 mmol, 2.0 equiv) was added slowly at 0 °C. The reaction was stirred at 0 °C for 6 h. The reaction mixture was diluted with CH_2Cl_2 and washed sequentially with 1 M HCl, 1 M $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography over silica gel eluting with hexane/EtOAc (40:1). The filtrate was concentrated in vacuo to give **3d** as a white solid (2.3 g, 88%).

R_f 0.20 (Hexane/EtOAc = 20/1). White solid (2.3 g, 88%). Mp = 45 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.33 (s, 9H), 6.98 (d, *J* = 8.2 Hz, 1H), 7.01 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.19 (td, *J* = 1.8, 8.4 Hz, 1H), 7.29-7.39 (m, 4H).

^{13}C NMR ($CDCl_3$, 150.92 MHz): δ 31.3, 34.9, 116.8 (q, *J* = 320.2 Hz), 119.7, 120.0, 120.6, 123.4, 124.8, 126.5, 129.4, 140.2, 140.3, 145.0, 148.4, 149.5. One carbon peak (CF_3) is overlapped with other carbon peaks.

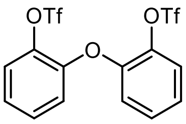
IR (ATR): 2970 w, 1604 w, 1587 w, 1495 m, 1458 w, 1420 s, 1366 w, 1302 w, 1274 m, 1246 m, 1200 s, 1167 m, 1154 m, 1134 s, 1118 m, 1096 m, 1077 m, 1042 w, 940 m, 904 m, 880 w, 859 m, 841 m, 764 m, 780 w, 760 s, 720 w, 705 w, 669 w.

MS m/z (% relative intensity): 522 (M^+, 36), 509 (12), 508 (20), 507 (100), 374 (10), 256 (16), 241 (12), 240 (23), 225 (29), 57 (14).

HRMS (EI): Calcd for $C_{18}H_{16}F_6O_7S_2$ 522.0242, Found 522.0242.

Ditriflates **3a** and **3c**-**3h** were prepared according to this procedure using the corresponding diaryl ethers.

Oxybis(2,1-phenylene) bis(trifluoromethanesulfonate) (3a).



R_f 0.29 (Hexane/EtOAc = 10/1), Colorless oil (3.7 g, 75%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.03 (dd, *J* = 1.8, 8.3 Hz, 2H), 7.21-7.25 (m, 2H), 7.32-7.36 (m, 2H), 7.40 (dd, *J* = 1.4, 8.3 Hz, 2H).

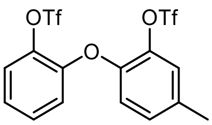
IR (ATR): 2955 w, 1921 w, 1600 w, 1493 m, 1457 w, 1423 m, 1274 m, 1249 m, 1203 s, 1134 s, 1094 m, 1035 w, 940 w, 905 m, 888 m, 849 m, 793 m, 759 m, 714 w.

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 118.8 (q, *J* = 321.1 Hz), 120.2, 123.6, 125.3, 129.6, 140.4, 147.9.

MS m/z (% relative intensity): 466 (M^+, 41), 200 (72), 184 (100), 172 (16), 171 (26).

HRMS (EI): Calcd for $C_{14}H_8F_6O_7S_2$ 465.9616, Found 465.9612.

2-(4-Methyl-2-(((trifluoromethyl)sulfonyl)oxy)phenoxy)phenyl trifluoromethanesulfonate (3c).



R_f 0.29 (Hexane/EtOAc = 10/1). White solid (4.1 g, 74%). Mp = 52 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.39 (s, 3H), 6.93-6.99 (m, 2H), 7.14 (dd, *J* = 1.4, 8.3 Hz, 1H), 7.17 – 7.21 (m, 2H), 7.31 (td, *J* = 1.4, 7.8 Hz, 1H), 7.37 (dd, *J* = 1.4, 8.3 Hz, 1H).

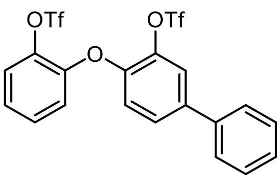
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 20.9, 118.8 (q, *J* = 318.2 Hz), 118.9 (q, *J* = 321.1 Hz), 119.6, 120.4, 123.5, 123.8, 124.8, 129.5, 130.2.136.1, 140.1, 140.2, 145.2, 148.4.

IR (ATR): 2934 w, 1606 w, 1509 m, 1493 m, 1457 w, 1415 s, 1267 m, 1246 m, 1206 s, 1152 m, 1134 s, 1091 s, 1035w, 1013 w, 952 m, 903 m, 879 w, 851 s, 832 s, 775 m, 760 s, 734 w, 717 w, 700 w.

MS m/z (% relative intensity): 480 (M^+, 42), 347 (11), 215 (11), 214 (79), 199 (14), 198 (100), 186 (13), 185 (15).

HRMS (EI): Calcd for $C_{15}H_{10}F_6O_7S_2$ 479.9772, Found 479.9769.

2-((3-(((Trifluoromethyl)sulfonyl)oxy)-[1,1'-biphenyl]-4-yl)oxy)phenyl trifluoromethanesulfonate (3e).



R_f 0.22 (Hexane/EtOAc = 20/1). White solid (5.8 g, 78%). Mp = 58 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.10 (d, *J* = 8.7 Hz, 2H), 7.24 (td, *J* = 1.4, 7.8 Hz, 1H), 7.36 (td, *J* = 1.4, 7.8 Hz, 1H), 7.40-7.42 (m, 2H), 7.45-7.49 (m, 2H), 7.52-7.55 (m, 3H), 7.58 (d, *J* = 2.3 Hz, 1H).

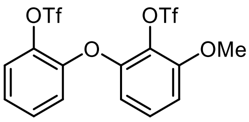
[13]C NMR ($CDCl_3$, 150.92 MHz): δ 118.9 (q, *J* = 321.3 Hz), 120.2, 120.4, 122.0, 123.6, 125.3, 127.2, 128.0, 128.4, 129.3, 129.7, 138.6, 139.2, 140.4, 140.6, 147.0, 148.0. One carbon peak (CF_3) is overlapped with other carbon peaks.

IR (ATR): 3072 w, 1603 w, 1514 w, 1487 m, 1455 w, 1421 s, 1302 w, 1277 m, 1248 m, 1206 s, 1136 s, 1094 m, 1046 w, 1025 w, 986 w, 950 w, 922 m, 894 s, 849 m, 805 s, 781 w, 762 s, 741 w, 700 m, 659 w.

MS m/z (% relative intensity): 543 (15), 542 (M^+, 64), 409 (10), 277 (14), 276 (72), 261 (19), 260 (100), 248 (18), 247 (21), 128 (17).

HRMS (EI): Calcd for $C_{20}H_{12}F_6O_7S_2$ 541.9929, Found 541.9925.

2-(3-Methoxy-2-(((trifluoromethyl)sulfonyl)oxy)phenoxy)phenyl trifluoromethanesulfonate (3f).



R_f 0.086 (Hexane/EtOAc = 20/1). Pale yellow oil (3.2 g, 53%).

[1]H NMR ($CDCl_3$, 399.78 MHz): δ 3.95 (s, 3H), 6.55 (dd, *J* = 1.4, 8.2 Hz, 1H), 6.83 (dd, *J* = 1.4, 8.7 Hz, 1H), 7.04 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.20-7.26 (m, 2H), 7.33 (td, *J* = 1.4, 7.8 Hz, 1H), 7.39 (dd, *J* = 1.8, 8.2 Hz, 1H).

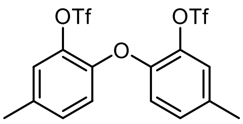
[13]C NMR ($CDCl_3$, 100.53 MHz): δ 56.7, 108.4, 111.1, 118.8 (q, *J* = 311.5 Hz), 118.9 (q, *J* = 328.7 Hz), 120.5, 123.5, 125.3, 128.9, 129.6, 130.1, 140.5, 147.8, 149.0, 153.3.

IR (ATR): 1912 w, 1602 w, 1493 m, 1479 m, 1459 w, 1421 s, 1297 w, 1260 m, 1204 s, 1134 s, 1097 s, 1082 m, 1034 w, 947 w, 884 s, 817 m, 780 m, 755 m, 686 w, 668 w, 657 w.

MS m/z (% relative intensity): 496 (M^+, 32), 364 (16), 363 (100), 230 (51), 215 (16), 214 (96), 202 (10), 187 (57).

HRMS (EI): Calcd for $C_{15}H_{10}F_6O_8S_2$ 495.9721, Found 495.9718.

Oxybis(5-methyl-2,1-phenylene) bis(trifluoromethanesulfonate) (3g).



R_f 0.37 (Hexane/EtOAc = 10/1). White solid (4.0 g, 54%). Mp = 98 °C.

[1]H NMR ($CDCl_3$, 399.78 MHz): δ 2.37 (s, 6H), 6.89 (d, *J* = 8.7 Hz, 2H), 7.11 (dd, *J* = 1.4, 8.4 Hz, 2H), 7.17 (dd, *J* = 1.4 Hz, 2H).

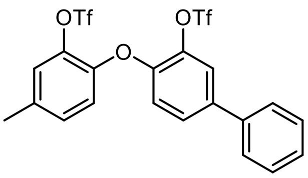
[13]C NMR ($CDCl_3$, 100.53 MHz): δ 20.8, 118.8 (q, *J* = 320.1 Hz), 119.8, 123.7, 130.1, 135.5, 140.0, 145.7.

IR (ATR): 2936 w, 1503 m, 1415 m, 1265 m, 1246 m, 1209 s, 1135 s, 1089 s, 1011 w, 949 s, 874 m, 851 s, 817 s, 765 w, 725 w, 701 m.

MS m/z (% relative intensity): 494 (M^+, 39), 346 (14), 229 (12), 228 (78), 213 (30), 212 (100), 200 (10), 199 (10), 198 (14), 185 (11).

HRMS (EI): Calcd for $C_{16}H_{12}F_6O_7S_2$ 493.9929, Found 493.9931.

4-(4-Methyl-2-(((trifluoromethyl)sulfonyl)oxy)phenoxy)-[1,1'-biphenyl]-3-yl trifluoromethanesulfonate (3h).



R_f 0.37 (Hexane/EtOAc = 10/1). Colorless oil (3.1 g, 81%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.40 (s, 3H), 7.00 (d, J = 8.2 Hz, 1H), 7.04 (d, J = 8.7 Hz, 1H), 7.15-7.17 (m, 1H), 7.21 (d, J = 1.4 Hz. 1H), 7.37-7.41 (m, 1H), 7.44-7.56 (m, 6H).

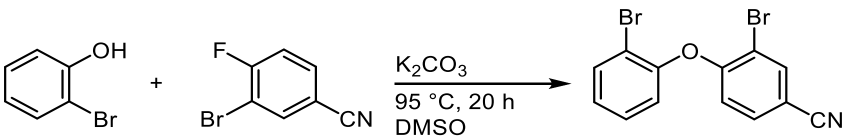
^{13}C NMR ($CDCl_3$, 150.92 MHz): δ 20.9, 118.8 (q, J = 321.4 Hz), 118.9 (q, J = 321.4 Hz), 119.8, 120.4, 122.0, 123.8, 127.1, 127.9, 128.3, 129.2, 130.2, 136.1, 138.6, 138.7, 140.2, 140.3, 145.3, 147.5.

IR (ATR): 3064 w, 1901 w, 1573 w, 1506 m, 1486 m, 1425 s, 1276 m, 1246 m, 1207 s, 1137 s, 1095 m, 1045 w, 1004 w, 950 m, 924 m, 855 m, 836 m, 801 w, 761 m, 698 w.

MS m/z (% relative intensity): 557 (13), 556 (M^+, 56), 291 (14), 290 (67), 275 (20), 274 (100), 262 (11), 261 (12), 128 (13).

HRMS (EI): Calcd for $C_{21}H_{14}F_6O_7S_2$ 556. 0085, Found 556.0082.

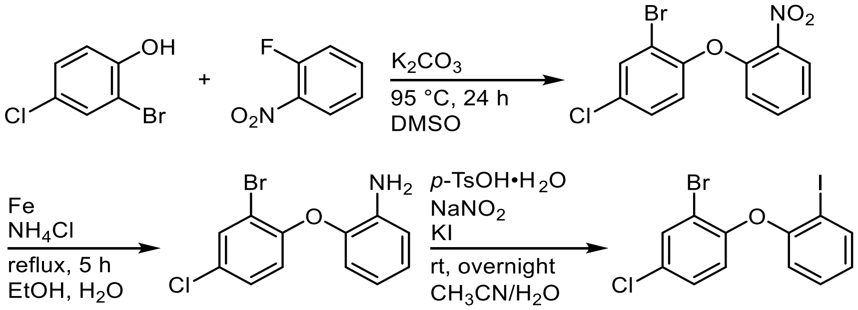
3-Bromo-4-(2-bromophenoxy)benzonitrile (3i). [CAS: 1553446-38-0]



K_2CO_3 (6.9 g, 50 mmol, 2.0 equiv) was added to a solution of 2-bromophenol (4.3 g, 25 mmol, 1.0 equiv) and 3-bromo-4-fluorobenzonitrile (5.0 g, 25 mmol, 1.0 equiv) in dehydrated DMSO (160 mL) and the suspension was stirred at 95 °C in 20 h. After cooling to room temperature, water (60 mL) was added to the reaction mixture, and the resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was then removed under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc (10/1). The filtrate was concentrated in vacuo to give **3i** as a white solid (4.8 g, 55%). The spectroscopic data of this material was in agreement with those reported in the literature.[20]

Dibromides **3b**, **3o** and **3p** were prepared according to this method.

2-Bromo-4-chloro-1-(2-iodophenoxy)benzene (3k).



K_2CO_3 (20 g, 150 mmol, 2.0 equiv) was added to a solution of 2-bromo-4-chlorophenol (15 g, 73 mmom, 1.0

equiv) and 1-fluoro-2-nitrobenzene (10 g, 73 mmol, 1.0 equiv) in dehydrated DMSO (250 mL) and suspension was stirred at 95 °C for 24 h. After cooling to room temperature, water (50 mL) was added to the reaction mixture, and the resulting mixture was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was then removed under reduced pressure to give 2-bromo-4-chloro-1-(2-nitrophenoxy)benzene as a pale yellow solid.

The crude product was dissolved in EtOH (81 mL) and H_2O (81 mL), and Fe powder (12 g, 220 mmol) and NH_4Cl (12 g, 220 mmol) were then added. The reaction mixture was refluxed for 5 h. After cooling to room temperature, the mixture was filtrated through a pad of Celite and the filtrate was concentrated in vacuo. To the residue, brine (100 mL) was added, and the mixture was extracted with EtOAc (3 × 100 mL). The combined organic extracts were dried over $MgSO_4$, and the solvent was removed under reduced pressure to give an aniline derivative. This product was used for the next step without further purification.

To a solution of the aniline intermediate in acetonitrile (200 mL), *p*-TsOH•H_2O (34 g, 180 mmol) was added. After cooling to 0 °C, a solution of $NaNO_2$ (8.1 g, 120 mmol) and KI (25 g, 150 mmol) in H_2O (120 mL) was added dropwise, and the resulting mixture was stirred at room temperature overnight. The reaction was quenched by addition of saturated aqueous solution of $NaHCO_3$ (50 mL). Following the extraction with EtOAc (3 × 100 mL), the combined organic extracts were washed with $Na_2S_2O_3$ aq. (50 mL) and dried over $MgSO_4$. The solvent was then removed in vacuo to give the crude product, which was purified by column chromatography over silica gel eluting with hexane to give **3k** (8.0 g, 27% over three steps).

R_f 0.29 (Hexane). Colorless oil (8.0 g, 27% over three steps).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 6.74 (d, *J* = 9.2 Hz, 1H), 6.79 (dd, *J* = 1.4, 7.8 Hz, 1H), 6.90 (td, *J* = 1.4, 7.8 Hz, 1H), 7.21 (dd, *J* = 2.7, 8.7 Hz, 1H),7.30 (m, 1H), 7.64 (d, *J* = 2.7 Hz, 1H), 7.87 (dd, *J* = 1.4, 7.8 Hz, 1H).

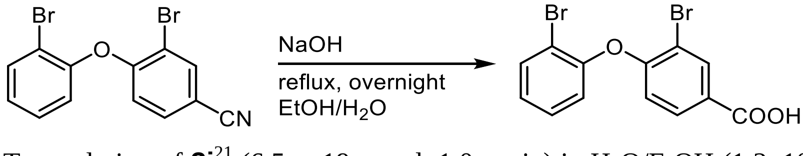
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 88.3, 115.0, 118.8, 120.2, 126.0, 128.8, 129.6, 129.9, 133.6, 140.3, 152.4, 155.8.

IR (ATR): 3066 w, 1916 w, 1571 w, 1492 m, 1461 s, 1425 m, 1383 m, 1254 m, 1209 s, 1137 m, 1095 m, 1043 m, 1020 m, 941 w, 906 m, 888 m, 850 m, 795 w, 761 s, 691 w.

MS m/z (% relative intensity): 412 (12), 410 (M^+, 45), 408 (36), 204 (32), 203 (16), 202 (100), 139 (18), 76 (18).

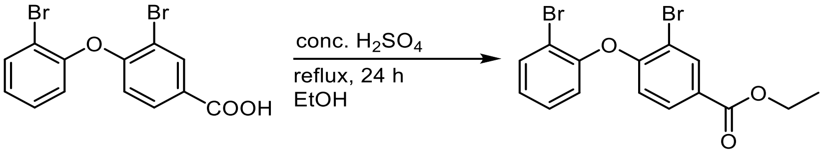
HRMS (EI): Calcd for $C_{12}H_7BrClIO$ 407.8413, Found 407.8412.

3-Bromo-4-(2-bromophenoxy)benzoic acid.



To a solution of **3i**[21] (6.5 g, 19 mmol, 1.0 equiv) in H_2O/EtOH (1:2, 100 mL), NaOH (19 g, 460 mmol, 25 equiv) was adeded. The resulting solution was refluxed overnight. After being cooled to room temperature, the mixture was evaporated to remove EtOH. The resulting mixture was diluted with H_2O (100 mL), cooled to 0 °C and acidified to pH 1 with conc. HCl aq. The generated white solid was collected by filtration, washed with H_2O, and dried in vacuo to give 3-bromo-4-(2-bromophenoxy)benzoic acid as a white solid (6.2 g, 91%).

Ethyl 3-bromo-4-(2-bromophenoxy)benzoate (3l).



A few drops of conc. H_2SO_4 was added to a solution of 3-bromo-4-(2-bromophenoxy)benzoic acid (3.0 g, 8.1 mmol) in ethanol (100 mL), and the resulting mixture was refluxed for 24 h. After the solvent was evaporated in vacuo, the residue was basified with sat. $NaHCO_3$ aq. until the pH of the solution becomes ~8. The mixture was the extracted with Et_2O (3 × 30 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and evaporated in vacuo to give the crude product, which was purified by column chromatography over silica gel eluting with hexane/EtOAc (10/1). The filtrate was concentrated in vacuo to **3l** as a pale yellow solid (900 mg, 28%).

R_f 0.31 (Hexane/EtOAc = 10/1). Pale yellow solid (900 mg, 28%). Mp = 82 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.39 (t, *J* = 7.3 Hz, 3H), 4.37 (q, *J* = 7.3 Hz, 2H), 6.68 (d, *J* = 8.7 Hz, 1H), 7.04 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.13 (td, *J* = 1.4, 7.8 Hz, 1H), 7.34 (td, *J* = 1.4, 7.8 Hz, 1H), 7.67 (dd, *J* = 1.4, 7.8 Hz, 1H), 7.89 (dd, *J* = 2.3, 8.7 Hz, 1H), 8.33 (d, *J* = 2.3 Hz, 1H).

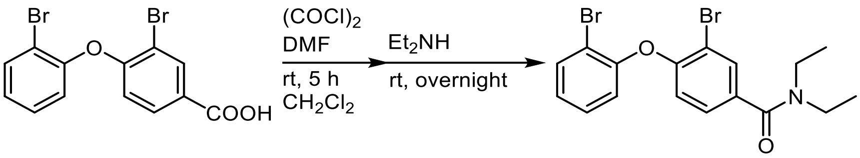
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.5, 61.4, 112.9, 115.6, 116.7, 121.8, 126.6, 126.7, 129.1, 130.3, 134.4, 135.5, 152.1, 157.5, 165.0.

IR (ATR): 2983 w, 2902 w, 1708 m, 1599 w, 1575 w, 1485 w, 1465 m, 1402 w, 1367 w, 1281 s, 1262 s, 1238 s, 1202 m, 1124 m, 1108 m, 1042 m, 1025 m, 951 w, 901 m, 873 m, 829 m, 797 w, 760 s, 680 m, 655 m.

MS m/z (% relative intensity): 402 (45), 401 (15), 400 (90), 398 (M^+, 46), 372 (13), 357 (50), 356 (17), 355 (100), 353 (52), 248 (14), 246 (14), 225 (11), 212 (16), 195 (16), 177 (13), 168 (22), 139 (30), 75 (10).

HRMS (EI): Calcd for $C_{15}H_{12}Br_2O_3$ 397.9153, Found 397.9151.

3-Bromo-4-(2-bromophenoxy)-*N*,*N*-diethylbenzamide (3m).



To a solution of 3-bromo-4-(2-bromophenoxy)benzoic acid (3.0 g, 8.1 mmol, 1.0 equiv), DMF (0.30 mL, 3.8 mmol, 0.47 equiv) in dehydrated CH_2Cl_2 (20 mL) and oxalyl chloride (1.0 mL, 12 mmol, 1.5 equiv) was added dropwise at 0 °C. The reaction mixture was then allowed to warm to room temperature and stirred for 5 h. Et_2NH (4.1 mL, 39 mmol, 4.8 equiv) was added slowly to the reaction mixture at 0 °C and it was stirred at room temperature overnight. The reaction mixture was concentrated under reduced pressure to give a crude product, which was purified by column chromatography over silica gel eluting with hexane/EtOAc (10/1) to give **3m** as a white solid (2.8 g, 80%).

R_f 0.14 (Hexane/EtOAc = 3/1). White solid (2.8 g, 80%). Mp = 59 °C.

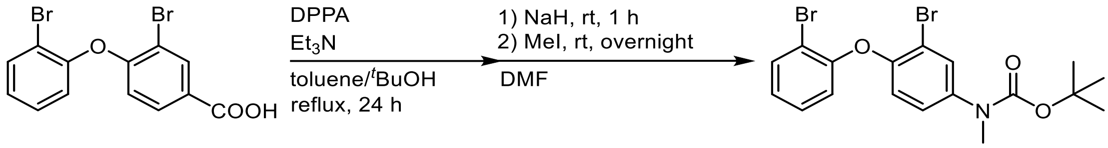
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.19 (br, 6H), 3.41 (br, 4H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.93 (dd, *J* = 1.5, 7.8 Hz, 1H), 7.07 (td, *J* = 1.4, 7.8 Hz, 1H), 7.25-7.32 (m, 2H), 7.66 (dd, *J* = 1.4, 7.8 Hz, 1H), 7.69 (d, *J* = 1.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 13.0, 14.3, 39.6, 43.6, 113.8, 114.9, 118.5, 120.6, 125.9, 127.1, 129.0, 132.3, 133.8, 134.2, 152.8, 154.3, 169.3.

IR (ATR): 2972 w, 2940 w, 1617 s, 1566 w, 1468 m, 1450 s, 1427 m, 1381 w, 1364 w, 1308 m, 1290 m, 1258 s, 1240 s, 1217 m, 1148 w, 1096 m, 1067 w, 1045 m, 1030 w, 944 w, 894 m, 865 w, 822 w, 810 w, 789 m, 767 s, 757 s, 728 w, 714 w, 687 w, 658 w.

MS m/z (% relative intensity): 429 (17), 428 (33), 427 (33), 426 (59), 425 (M^+, 17), 424 (28), 357 (49), 356 (15), 355 (100), 353 (51), 248 (11), 246 (11), 195 (12), 139 (23).

tert **-Butyl (3-bromo-4-(2-bromophenoxy)phenyl)(methyl)carbamate (3n).**



A solution of 3-bromo-4-(2-bromophenoxy)benzoic acid (3.0 g, 8.1 mmol, 1.0 equiv) in toluene/*t*-BuOH (1/1, 100 mL) was treated with Et_3N (1.3 mL, 9.4 mmol, 1.2 equiv), 3 Å molecular sieves (9.6 g) and diphenyl phosphpryl azide (DPPA, 2.0 mL, 9.6 mmol, 1.2 equiv). The reaction mixture was heated at reflux for 24 h and then cooled to room temperature. The solid was filtered off by passing the solution through a Celite Pad and the solvent was removed in vacuo. The residue was dissolved in EtOAc (60 mL), and the solution was washed with HCl (1 M, 2 ×50 mL), sat. $NaHCO_3$ aq. (2 × 50 mL), dried over $MgSO_4$, and concentrated. Silica gel chromatography with hexane/EtOAc (10/1) afforded *t*-butyl (3-bromo-4-(2-bromophenoxy)phenyl)carbamate as a pale yellow oil (3.0 g, 84%).

(3-Bromo-4-(2-bromophenoxy)phenyl)carbamate (3.0 g, 6.8 mmol, 1.0 equiv) was added slowly at 0 °C to a suspension of NaH (60% in mineral oil, 410 mg, 10 mmol, 1.5 equiv) in DMF (70 mL). After stirring the mixture at room temperature for 1 h, MeI (2.2 mL, 35 mmol, 5.2 equiv) was added. The reaction mixture was stirred at room temperature overnight, quenched with H_2O, and extracted with CH_2Cl_2 (2 × 30 mL). The combined organic extracts were dried over $MgSO_4$ and then evaporated. The residue was purified by silica gel chromatography with hexane/EtOAc (10/1) to give *t*-butyl **3n** as a white solid (1.8 g, 58%).

R_f 0.49 (Hexane/EtOAc = 5/1).White solid (1.8 g, 58%). Mp = 64 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.47 (s, 9H), 3.25 (s, 3H), 6.78-6.85 (m, 2H), 7.01 (td, *J* = 1.4, 7.8 Hz, 1H), 7.14 (dd, *J* = 2.3, 8.7 Hz, 1H), 7.22-7.26 (m, 1H), 7.55 (dd, *J* = 2.8 Hz, 1H), 7.63 (dd, *J* = 1.4, 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 28.4, 37.4, 80.9, 113.8, 114.1, 119.3, 119.4, 125.1, 125.9, 128.8, 130.9, 134.0, 140.7, 150.7, 153.5, 154.6.

IR (ATR): 3074 w, 2981 w, 1687 s, 1596 w, 1576 w, 1484 m, 1469 s, 1446 m, 1429 m, 1361 s, 1255 s, 1232 m, 1180 w, 1146 s, 1106 s, 1044 m, 1030 m, 985 w, 881 m, 840 m, 821 m, 759 s, 723 w, 687 w, 665 w.

MS m/z (% relative intensity): 403 (49), 402 (16), 401 (100), 400 (10), 399 (51), 359 (34), 358 (14), 357 (68), 356 (14), 355 (37), 202 (26), 200 (27), 149 (17), 57 (80.)

HRMS (EI): Calcd for $C_{18}H_{19}Br_2NO_3$ 454.9732, Found 454.9728.

2.4.3 General Procedures for the Pd-Catalyzed Synthesis of Cyclic Diarylborinic Acids 1

Method A: Procedure for the Pd-Catalyzed Synthesis of Cyclic Diarylborinic Acids 1 Using Ditriflates

DPEPhos (54 mg, 0.10 mmol, 0.20 equiv), ditriflate **3a** (230 mg, 0.50 mmol, 1.0 equiv), Et_3N (230 mg, 2.5 mmol, 5.0 equiv) and $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv) were added to an oven-dried-10-mL-sample vial with a Teflon-sealed screwcap under a gentle stream of N_2, and stirred for 15 min at room temperature. **4** (110 mg, 1.0 mmol, 2.0 equiv) in THF (2.0 mL) was added, and the cap was applied to seal the vial. The reaction mixture was then stirred at 65 °C for 15 h. After the reaction mixture was cooled to room temperature, MeOH (1.5 mL) was added and the mixture was stirred under N_2 at room temperature for 1.0 h. The crude mixture was concentrated under reduced pressure, and CH_2Cl_2 (10 mL) and a saturated aqueous solution of NH_4Cl (10 mL) were added. The solution was stirred for 1.5 h at room temperature. The mixture was then extracted with CH_2Cl_2 (30 mL × 3). The combined organic extracts were washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel with hexane/EtOAc (10:1) as the eluent to give pure product **1a** (89 mg, 91%).

Method B: Procedure for the Pd-Catalyzed Synthesis of Cyclic Diarylborinic Acids 1 Using Dibromides

CyJohnPhos (35 mg, 0.10 mmol, 0.20 equiv), dibromide **3b** (200 mg, 0.50 mmol, 1.0 equiv), KI (42 mg, 0.25 mmol, 0.50 equiv), Et_3N (230 mg, 2.5 mmol, 5.0 equiv) and $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv) were added to an oven-dried-10-mL-sample vial with a Teflon-sealed screwcap under a gentle stream of N_2, and stirred for 15 min at room temperature. **4** (110 mg, 1.0 mmol, 2.0 equiv) in THF (2 mL) was added, and the cap was applied to seal the vial. The reaction mixture was then stirred at 65 °C for 15 h. After the reaction mixture was cooled to room temperature, MeOH (1.5 mL) was added and the reaction mixture was stirred under N_2 at room temperature for 1.0 h. The crude mixture was concentrated under reduced pressure, and CH_2Cl_2 (10 mL) and as saturated aqueous solution of NH_4Cl (10 mL) were added. The solution was stirred for 1.5 h at room temperature. The mixture was then extracted with CH_2Cl_2 (30 mL × 3). The combined organic extracts were washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and purified by flash column chromatography on silica gel eluting with hexane/EtOAc (10:1). The filtrate was concentrated in vacuo to give pure product **1b** (99 mg, 75%).

2.4.4 A Procedure for the Gram Scale Synthesis of 1i

CyJohnPhos (480 mg, 1.4 mmol, 0.16 equiv), dibromide **3i** (3.0 g, 8.9 mmol, 1.0 equiv), KI (570 mg, 3.4 mmol, 0.40 equiv), Et_3N (3.5 mg, 34 mmol, 4.0 equiv) and $Pd(OAc)_2$ (150 mg, 0.68 mmol, 0.080 equiv) were added to an oven-dried-190-mL-sample vial with a Teflon-sealed screwcap under a gentle stream of N_2, and stirred for 15 min at room temperature. **4** (1.9 g, 17 mmol, 2.0 equiv) in THF (15 mL) was then added, and the cap was applied to seal the vial. The reaction mixture was stirred at 65 °C for 24 h. After the reaction mixture was cooled to room temperature, MeOH (30 mL) was added and the reaction mixture was stirred under N_2 at room temperature for 2.0 h. The crude mixture was concentrated under reduced pressure, and then CH_2Cl_2 (100 mL) and a saturated aqueous solution of NH_4Cl (100 mL) were added. The solution was stirred for 2.0 h at room temperature. The mixture was extracted with CH_2Cl_2 (100 mL × 3). The combined organic extracts were washed with brine (100 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and purified by flash column chromatography on silica gel eluting with hexane/EtOAc (10:1). The filtrate was concentrated in vacuo to give pure product **1i** (1.4 g, 73%).

2.4.5 General Procedure for the Suzuki-Miyaura Cross-Coupling Reaction with Cyclic Diarylborinic Acids **1i**[3e]

Cyclic diarylborinic acid **1i** (55 mg, 0.25 mmol, 1.0 equiv), $Pd_2(dba)_3$ (3.4 mg, 0.0038 mmol, 0.015 equiv), $^tBu_3P$•HBF_4 (2.6 mg, 0.0090 mmol, 0.036 equiv) and Cs_2CO_3 (270 mg, 0.83 mmol, 3.3 equiv) were added to an oven-dried-10-mL-sample vial with a Teflon-sealed screwcap under a gentle stream of N_2. The vial was evacuated and refilled with N_2 three times, and then ^{t}AmOH (3.0 mL), H_2O (45 mg, 2.5 mmol, 10 equiv) and **5a** (120 mg, 0.50 mmol, 2.0 equiv) were added. The reaction was stirred for 1 h at room temperature prior to heating at 100 °C for 20 h. The reaction was then cooled to room temperature, and the crude product was filtered through a pad of Celite using EtOAc as the eluent. The filtrate was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel eluting with hexane/EtOAc (10:1). The filtrate was further purified by GPC to give pure product **6a** as a white solid (50 mg, 75%).

2.4.6 A Procedure for Suzuki-Miyaura Cross-Coupling Reaction with Borinate **1j**

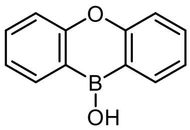
CyJohnPhos (35 mg, 0.10 mmol, 0.20 equiv), dibromide **3i** (200 mg, 0.50 mmol, 1.0 equiv), KI (42 mg, 0.25 mmol, 0.50 equiv), Et_3N (230 mg, 2.5 mmol, 5.0 equiv) and $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv) were added to an oven-dried-10 mL-sample vial with a Teflon-sealed screwcap under a gentle stream of N_2, and stirred for 15 min at room temperature. **4** (110 mg, 1.0 mmol, 2.0 equiv) in THF (2 mL) was then added, and the cap was applied to seal the vial. The reaction mixture was stirred at 65 °C for 15 h. After the reaction mixture was cooled to room temperature, 2-aminoethanol (122 mg, 2.0 mmol, 4.0 equiv) and THF (1.5 mL) were added and stirred under N_2 at room temperature for 24 h. The resulting mixture was washed with EtOAc (50 mL) and then with CH_2Cl_2 (10 mL) and the filtrate was concentrated in vacuo. The crude **1j**, $Pd_2(dba)_3$ (6.8 mg, 0.0076 mmol, 0.015 equiv), $^tBu_3P$•HBF_4 (5.2 mg, 0.018 mmol, 0.036 equiv) and Cs_2CO_3 (540 mg, 1.7 mmol, 3.3 equiv) was added to an oven-dried-10 mL-sample vial with a Teflon-sealed screwcap under a gentle stream of nitrogen. The vial was evacuated and refilled with N_2 three times. ^{t}AmOH (5.0 mL), H_2O (90 mg, 5.0 mmol, 10 equiv) and **5a** (240 mg, 1.0 mmol, 2.0 equiv) were added. The reaction mixture was stirred for 1 h at room temperature prior to heating at 100 °C for 24 h. The reaction was cooled to room temperature, and the crude was filtered through a pad of Celite eluting with EtOAc. The filtrate was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel eluting with hexane/EtOAc (10:1). The filtrate was further purified by GPC to give pure product **6a** as a white solid (69 mg, 51% for two steps).

2.4.7 A Procedure for the Synthesis of 10-Mesityl-10*H*-dibenzo[*b,e*][1,4]oxaborinine (**7a**)

DPEPhos (32 mg, 0.060 mmol, 0.20 equiv), **1a** (140 mg, 0.30 mmol, 1.0 equiv), Et_3N (140 mg, 1.5 mmol, 5.0 equiv) and $Pd(OAc)_2$ (6.7 mg, 0.030 mmol, 0.10 equiv) were added to an oven-dried-10 mL-sample vial with a Teflon-sealed screwcap under a gentle stream of N_2, and stirred for 15 min at room temperature. **4** (68 mg, 0.60 mmol, 2.0 equiv) in THF (2 mL) was added, and the cap was applied to seal the vial. The reaction mixture was then stirred at 65 °C for 15 h. After the reaction mixture was cooled to room temperature, it was transferred to a dry 30 mL two-necked flask under N_2, and THF (10 mL) was added. Mesityllithium[22] (ca. 0.3 M in hexane, 5.0 mL, 1.5 mmol, 5.0 equiv) was added slowly to the solution at -78 °C. The suspension was allowed to warm to room temperature and then stirred for 24 h. The reaction mixture was poured into ice/water (50 mL), and extracted with CH_2Cl_2 (30 mL × 3). The combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was then removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel eluting with hexane/CH_2Cl_2 (20:1). The filtrate was concentrated in vacuo to give a pale yellow solid. This solid was washed with hexane (20 mL) to afford **7a** as a white solid (47 mg, 53%).

2.4.8 Spectroscopic Data for Products

10*H*-Dibenzo[*b,e*][1,4]oxaborinin-10-ol (1a). [CAS: 19014-28-9]



Method A was used. R_f 0.20 (Hexane/EtOAc = 10/1). White solid (72 mg, 76%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 7.28 (t, *J* = 7.3 Hz, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.67 (t, *J* = 8.3 Hz, 2H), 8.15 (d, *J* = 7.3 Hz, 2H), 9.88 (s, 1H).

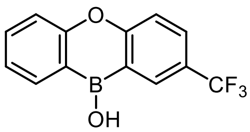
^{13}C NMR (CD_2Cl_2, 100.53 MHz): δ 117.1, 120.3, 122.2, 132.0, 133.3, 160.8.

HRMS (EI): Calcd for $C_{12}H_9BO_2$ 196.0696, Found 190.0696.

^{11}B NMR (DMSO-d_6, 128.27 MHz): 38.2.

Spectroscopic data was in agreement with the reported values.[3d,e]

2-(Trifluoromethyl)-10*H*-dibenzo[*b,e*][1,4]oxaborinin-10-ol (1b).



Method B was used. R_f 0.23 (Hexane/EtOAc = 10/1). Pale yellow solid (99 mg, 75%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 7.33 (t, *J* = 7.4 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 8.9 Hz, 1H), 7.69-7.73 (m, 1H), 7.97 (dd, *J* = 1.8, 8.8 Hz, 1H), 8.15 (d, *J* = 7.4 Hz, 1H), 8.53 (s, 1H), 10.2 (s, 1H).

^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 117.3, 118.5, 120.1, 120.2 (q, *J* = 3.8 Hz), 120.4, 120.5 (q, *J* = 6.6 Hz), 122.8 (q, *J* = 31 Hz), 124.5 (q, *J* = 271 Hz), 129.6, 132.0, 133.8, 160.6, 162.4.

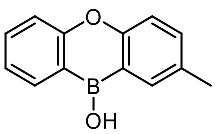
^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 36.9.

IR (ATR): 3414 w, 2360 w, 1629 w, 1610 m, 1586 w, 1492 w, 1450 m, 1400 w, 1361 m, 1297 s, 1279 m, 1229 m, 1200 w, 1156 m, 1137 m, 1106 s, 1086 s, 1069 m, 1029 w, 964 w, 917 w, 863 w, 829 m, 756 s, 702 w, 664 m.

MS m/z (% relative intensity): 265 (13), 264 (M^+, 76), 263 (26), 255 (11), 248 (16), 247 (29), 236 (38), 235 (12), 217 (39), 170 (12), 84 (24), 66 (26).

HRMS (EI): Calcd for $C_{13}H_8BF_3O_2$ 264.0569, Found 264.0572.

2-Methyl-10*H*-dibenzo[*b,e*][1,4]oxaborinin-10-ol (1c). [CAS: 1608475-76-8]



Method A was used. R_f 0.20 (Hexane/EtOAc = 10/1). White solid (78 mg, 74%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 2.38 (s, 3H), 7.24-7.28 (m, 1H), 7.32 (d, *J* = 8.7 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.47 (dd, *J* = 2.3, 8.7 Hz, 1H), 7.63-7.67 (m, 1H), 7.92 (d, *J* = 1.8 Hz, 1H), 8.13 (dd, *J* = 1.3, 7.3 Hz, 1H), 9.77 (s, 1H).

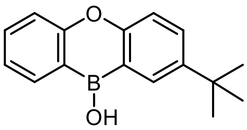
^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 20.5, 116.9, 117.1, 120.1, 120.3, 122.0, 130.9, 131.5, 131.9, 133.1, 134.2, 159.0, 160.8.

^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 37.9.

HRMS (EI): Calcd for $C_{13}H_{11}BO_2$ 210.0852, Found 210.0854.

Spectroscopic data was in agreement with the reported values.[3d]

2-(*tert* -Butyl)-10*H*-dibenzo[*b,e*][1,4]oxaborinin-10-ol (1d). [CAS: 1608475-80-4]



Method A was used. R_f 0.37 (Hexane/EtOAc = 10/1). Colorless oil (86 mg, 68%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 1.35 (s, 9H), 7.26 (t, *J* = 7.1 Hz, 1H), 7.35 (d, *J* = 9.0 Hz, 1H), 7.40 (t, *J* = 8.3 Hz, 1H), 7.62-7.67 (m, 1H), 7.71 (dd, *J* = 2.7, 8.9 Hz, 1H), 8.12 (dd, *J* = 1.4, 7.3 Hz, 1H), 8.17 (d, *J* = 2.7 Hz, 1H), 9.80 (s, 1H).

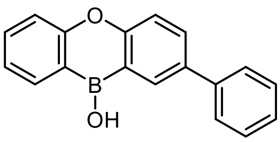
^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 31.4, 34.3, 116.7, 117.0, 119.5, 120.4, 122.0, 127.7, 130.8, 131.9, 133.1, 144.2, 158.9, 160.8.

^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 37.8.

HRMS (CI): Calcd for $C_{16}H_{17}BO_2$+H^+ 253.1401, Found 253.1397.

Spectroscopic data was in agreement with the reported values.[3d]

2-Phenyl-10*H*-dibenzo[*b,e*][1,4]oxaborinin-10-ol (1e).



Method A was used. R_f 0.29 (Hexane/EtOAc = 10/1). White solid (79 mg, 58%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 7.30 (d, *J* = 7.3 Hz, 1H), 7.37 (d, *J* = 7.3 Hz, 1H), 7.44-7.53 (m, 4H), 7.66-7.71 (m, 1H), 7.74 (d, *J* = 7.3 Hz, 2H), 7.98 (dd, *J* = 2.3, 8.7 Hz, 1H), 8.15 (dd, *J* = 1.4, 7.3 Hz, 1H), 8.50 (d, *J* = 2.3 Hz, 1H), 9.96 (s, 1H).

^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 117.2, 117.8, 120.4, 120.5, 122.3, 126.5, 127.2, 129.0, 129.9, 131.6, 131.9, 133.3, 134.0, 139.7, 160.4, 160.8.

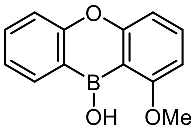
^{11}B NMR (DMSO-d_6, 128.27 MHz): 33.7.

IR (ATR): 3422 w, 3059 w, 3033 w, 2359 w, 1610 m, 1583 w, 1511 w, 1482 m, 1442 s, 1409 m, 1352 m, 1324 s, 1285 m, 1230 s, 1172 w, 1082 w, 1033 w, 953 w, 920 w, 897 w, 867 w, 833 w, 815 w, 756 s, 717 w, 681 m.

MS m/z (% relative intensity, CI): 274 (20), 273 (M^+, 97), 272 (46).

HRMS (CI): Calcd for $C_{18}H_{13}BO_2$+H^+ 273.1088, Found 273.1085.

1-Methoxy-10*H*-dibenzo[*b,e*][1,4]oxaborinin-10-ol (1f). [CAS: 1562342-67-9]



Method A was used. R_f 0.26 (Hexane/EtOAc = 10/1). White solid (49 mg, 43%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 3.93 (s, 3H), 6.82 (d, *J* = 8.2 Hz, 1H), 7.03 (d, *J* = 8.7 Hz, 1H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.60-7.68 (m, 2H), 7.98 (dd, *J* = 1.4, 7.4 Hz, 1H), 8.35 (s, 1H).

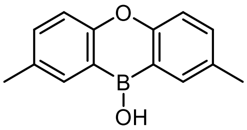
^{13}C NMR (CD_2Cl_2, 100.53 MHz): δ 55.9, 102.8, 110.8, 116.9, 122.3, 131.3, 133.1, 133.8, 161.0, 162.1, 164.8.

^{11}B NMR (DMSO-d_6, 128.27 MHz): 37.0.

HRMS (EI): Calcd for $C_{13}H_{11}BO_3$ 226.0801, Found 226.0802.

Spectroscopic data was in agreement with the reported values.[3d,e]

2,8-Dimethyl-10*H*-dibenzo[*b,e*][1,4]oxaborinin-10-ol (1g). [CAS: 1103654-00-7]



Method A was used. R_f 0.29 (Hexane/EtOAc = 10/1). White solid (84 mg, 75%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 2.37 (s, 6H), 7.30 (d, *J* = 8.7 Hz, 2H), 7.45 (dd, *J* = 2.2, 8.7 Hz, 2H), 7.91 (d, *J* = 2.1 Hz, 2H), 9.68 (s, 1H).

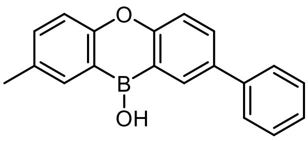
^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 20.5, 116.9, 120.0, 130.6, 131.5, 134.1, 159.0.

^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 37.3.

HRMS (EI): Calcd for $C_{14}H_{13}BO_2$ 224.1009, Found 224.1010.

Spectroscopic data was in agreement with the reported values.[3d]

2-Methyl-8-phenyl-10*H*-dibenzo[*b,e*][1,4]oxaborinin-10-ol (1h). [CAS: 1608475-86-0]



Method A was used. R_f 0.26 (Hexane/EtOAc = 10/1). White solid (100 mg, 70%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 2.40 (s, 3H), 7.34-7.39 (m, 2H), 7.48-7.52 (m, 4H), 7.73 (d, *J* = 7.8 Hz, 2H), 7.92 (d, *J* = 1.8 Hz, 1H), 7.96 (dd, *J* = 2.3, 8.7 Hz, 1H), 8.49 (d, *J* = 2.8 Hz, 1H), 9.88 (s, 1H).

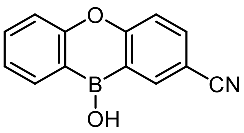
^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 20.5, 117.0, 117.8, 120.1, 120.4, 126.5, 127.1, 129.0, 129.9, 131.0, 131.5, 133.8, 134.3, 139.7, 159.0, 160.4. One carbon peak is overlapped with solvent peaks.[3d]

^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 35.5.

HRMS (EI): Calcd for $C_{19}H_{15}BO_2$ 286.1165, Found 286.1160.

Spectroscopic data was in agreement with the reported values.[3d]

10-Hydroxy-10*H*-dibenzo[*b,e*][1,4]oxaborinine-2-carbonitrile (1i).



Method B was used. R_f 0.22 (Hexane/EtOAc = 5/1). Pale yellow solid (80 mg, 72%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 7.35 (t, J = 6.9 Hz, 1H), 7.47 (d, J = 8.2 Hz, 1H), 7.60 (d, J = 8.7 Hz, 1H), 7.70-7.74 (m, 1H), 8.06 (dd, J = 2.3, 8.7 Hz, 1H), 8.14 (dd, J = 1.8, 8.0 Hz, 1H), 8.56 (d, J = 2.3 Hz, 1H), 10.2 (s, 1H).

^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 105.1, 117.4, 118.8, 119.0, 120.2, 121.2, 123.2, 132.1, 133.9, 135.9, 137.6 160.5, 162.8.

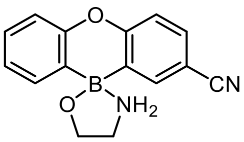
^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 36.5.

IR (ATR): 3444 m, 3079 w, 3053 w, 2924 w, 2853 w, 2542 w, 2301 w, 2231 m, 1925 w, 1806 w, 1729 w, 1604 s, 1579 m, 1485 m, 1463 w, 1441 s, 1415 s, 1385 s, 1317 s, 1305 s, 1234 s, 1188 m, 1133 m, 1109 s, 1082 s, 1027 m, 966 w, 943 m, 904 w, 867 m, 829 s, 744 s, 729 s, 691 s.

MS m/z (% relative intensity): 221 (M^+, 48), 220 (17), 193 (27).

HRMS (EI): Calcd for $C_{13}H_8BNO_2$ 221.0648, Found 221.0651.

10-(2-Aminoethoxy)-10*H*-dibenzo[*b,e*][1,4]oxaborinine-2-carbonitrile (1j).



CyJohnPhos (35 mg, 0.10 mmol, 0.20 equiv), **3i** (180 mg, 0.50 mmol, 1.0 equiv), KI (42 mg, 0.25 mmol, 0.50 equiv), Et_3N (230 mg, 2.5 mmol, 5.0 equiv) and $Pd(OAc)_2$ (11 mg, 0.050 mmol, 0.10 equiv) were added to an oven-dried-10 mL-sample vial with a Teflon-sealed screwcap under a gentle stream of N_2, and stirred for 15 min at room temperature. **4** (113.1 mg, 1.0 mmol, 2.0 equiv) in THF (2 mL) was added, and the cap was applied to seal the vial. The reaction mixture was then stirred at 65 °C for 15 h. After the reaction was cooled to room temperature, 2-aminoethanol (122 mg, 2.0 mmol, 4.0 equiv) and THF (1.5 mL) were added and the mixture was stirred under N_2 at room temperature for 24 h. The resulting mixture was washed with EtOAc (30 mL) and then with CH_2Cl_2 (10 mL). The filtrate was concentrated in vacuo, and the crude product was washed with EtOAc (10 mL) to give a gray solid (112 mg, 85%).

Gray solid (112 mg, 85%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 3.09 (m, 2H), 4.12 (t, J = 6.0 Hz, 2H), 5.98 (bs, 2H), 7.06 (m, 2H), 7.15 (m, 1H), 7.25 (m, 1H), 7.51 (d, J = 6.0 Hz, 1H), 7.64 (dd, J = 1.8, 8.2 Hz, 1H), 7.86 (d, J = 1.8 Hz, 1H).

^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 41.5, 65.0, 103.9, 115.3, 116.4, 120.1, 122.5, 127.8, 131.4, 132.9, 138.0, 156.6, 160.2.

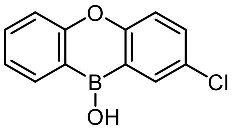
^{11}B NMR (DMSO-d_6, 128.27 MHz): 22.5.

IR (ATR): 3211 w, 2035 w, 2957 m, 2914 w, 2847 w, 1628 w, 1592 m, 1467 m, 1433 m, 1394 m, 1365 w, 1341 w, 1300 s, 1285 s, 1242 s, 1213 m, 1194 m, 1137 m, 1123 m, 1080 s, 1061 s, 958 m, 937 m, 889 m, 834 s, 822 s, 791 w, 754 s, 722 s, 676 w.

MS m/z (% relative intensity): 264 (M^+, 24). 263 (30), 234 (29), 233 (100), 232 (25). 204 (20), 203 (12).

HRMS (EI): Calcd for $C_{15}H_{13}BN_2O_2$ 264.1070, Found 264.1067.

2-Chloro-10*H*-dibenzo[*b*,*e*][1,4]oxaborinin-10-ol (1k).



Method B was used. R_f 0.26 (Hexane/EtOAc = 8/1). White solid (89 mg, 77%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 7.29 (t, J = 7.2 Hz, 1H), 7.42-7.48 (m, 2H), 7.66-7.70 (m, 2H), 8.11-8.14 (m, 2H), 10.0 (s, 1H).

^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 117.2, 119.6, 119.9, 122.1, 122.6, 126.5, 130.9, 132.0, 133.0, 133.6, 159.2, 160.7.

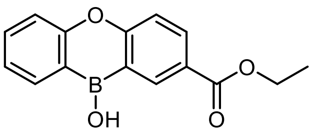
^{11}B NMR (DMSO-d_6, 128.27 MHz): 37.2.

IR (ATR): 3052 w, 1784 w, 1605 m, 1578 w, 1475 w, 1460 w, 1435 s, 1407 s, 1302 s, 1261 w, 1221 m, 1200 m, 1144 m, 1119 m, 1103 m, 1085 w, 1030 w, 977 w, 932 w, 894 w, 873 w, 859 w, 873 w, 859 w, 840 w, 818 m, 754 m, 715 m, 692 w, 662 w.

MS m/z (% relative intensity): 232 (27), 231 (19), 230 (M^+, 100), 229 (23).

HRMS (EI): Calcd for $C_{12}H_8BClO_2$ 230.0306, Found 230.0305.

Ethyl 10-hydroxy-10*H*-dibenzo[*b*,*e*][1,4]oxaborinine-2-carboxylate (1l).



Method B was used. R_f 0.20 (Hexane/EtOAc = 10/1). Pale yellow solid (109 mg, 81%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 1.35 (t, J = 7.3 Hz, 3H), 4.34 (q, J = 7.3 Hz, 2H), 7.32 (t, J = 7.3 Hz, 1H), 7.45 (d, J = 8.7 Hz, 1H), 7.50 (dd, J = 2.4, 8.7 Hz, 1H), 7.69 (td, J = 1.4, 8.7 Hz, 1H), 8.15-8.19 (m, 2H), 8.81 (d, J = 2.4 Hz, 1H), 10.2 (s, 1H).

^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 14.3, 60.6, 117.3, 117.7, 120.1, 120.3, 122.9, 123.7, 132.1, 133.6, 133.7, 134.4, 160.6, 163.5, 165.5.

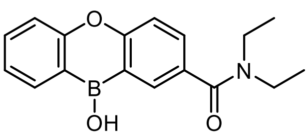
^{11}B NMR (DMSO-d_6, 128.27 MHz): 37.6.

IR (ATR): 3409 w, 3047 w, 2994 w, 2361 w, 1693 m, 1605 m, 1581 m, 1482 w, 1445 m, 1421 w, 1385 m, 1325 m, 1283 m, 1261 m, 1230 m, 1199 m, 1153 w, 1107 m, 1092 m, 1022 m, 944 m, 878 m, 835 m, 768 m, 754 s, 713 m, 671 w.

MS m/z (% relative intensity): 268 (M^+, 41), 267 (11), 240 (19), 224 (12), 223 (72), 222 (19), 195 (16), 167 (13).

HRMS (EI): Calcd for $C_{15}H_{13}BO_4$ 268.0907, Found 268.0909.

***N*,*N*-Diethyl-10-hydroxy-10*H*-dibenzo[*b*,*e*][1,4]oxaborinine-2-carboxamide (1m).**



Method B was used. R_f 0.25 (Hexane/EtOAc = 1/2). Pale yellow solid (96 mg, 65%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 1.12 (br, 6H), 3.34 (br, 4H), 7.30 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 8.2 Hz, 2H), 7.63-7.71 (m, 2H), 8.12-8.16 (m, 2H), 9.99 (s, 1H).

^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 13.0, 14.0, 43.0 (br, 2C), 117.1, 117.2, 119.9, 120.3, 122.5, 130.1, 131.1, 131.3, 131.9, 133.5, 160.7, 160.8, 169.8.

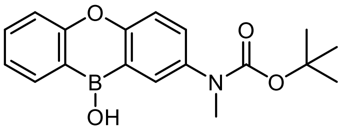
^{11}B NMR (DMSO-d_6, 128.27 MHz): 37.4.

IR (ATR): 3261 w, 2974 w, 2933 w, 2366 w, 1570 s, 1439 s, 1409 m, 1384 m, 1308 m, 1286 m, 1225 m, 1111 m, 1029 w, 950 w, 932 w, 822 m, 761 s, 704 w, 687 w, 658w.

MS m/z (% relative intensity, CI): 298 (16), 297 (25), 296 (100), 295 (M^+, 34), 286 (10).

HRMS (CI): Calcd for $C_{17}H_{18}BNO_3+H^+$ 296.1459, Found 296.1455.

tert **-Butyl (10-hydroxy-10*H*-dibenzo[*b,e*][1,4]oxaborinin-2-yl)(methyl)carbamate (1n)**.



Method B was used. R_f 0.09 (Hexane/EtOAc = 10/1). Brown solid (117 mg, 72%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 1.39 (s, 9H), 3.23 (s, 3H), 7.28 (t, J = 7.3 Hz, 1H), 7.41 (t, J = 8.7 Hz, 2H), 7.57 (dd, J = 2.8, 9.2 Hz, 1H), 7.65-7.69 (m, 1H), 7.98 (d, J = 2.8 Hz, 1H), 8.12 (dd, J = 1.4, 7.3 Hz, 1H), 9.87 (s, 1H)

^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 27.9, 37.3, 79.5, 117.1, 117.4, 119.9, 120.2, 122.3, 127.7, 131.3, 131.9, 133.3, 137.9, 154.0, 158.1, 160.8.

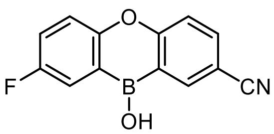
^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 33.8.

IR (ATR): 3360 w, 2978 w, 2927 w, 2340 w, 1668 s, 1609 m, 1582 w, 1486 m, 1442 s, 1378 s, 1318 s, 1302 m, 1254 m, 1223 m, 1156 s, 1114 s, 1028 w, 997 w, 919 w, 867 w, 836 m, 754 s.

MS m/z (% relative intensity): 325 (M^+, 10), 270 (16), 269 (100), 268 (25), 259 (15), 226 (10), 225 (67), 224 (39), 57 (33).

HRMS (EI): Calcd for $C_{18}H_{20}BNO_4$ 325.1485, Found 325.1487.

8-Fluoro-10-hydroxy-10*H*-dibenzo[*b,e*][1,4]oxaborinine-2-carbonitrile (1o).



Method B was used. R_f 0.09 (Hexane/EtOAc = 10/1). White solid (28 mg, 23%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 7.52-7.59 (m, 3H), 7.83 (dd, J = 2.8, 8.5 Hz, 1H), 8.06 (dd, J = 2.3, 8.6 Hz, 1H), 8.52 (d, J = 1.8 Hz, 1H), 10.3 (s, 1H).

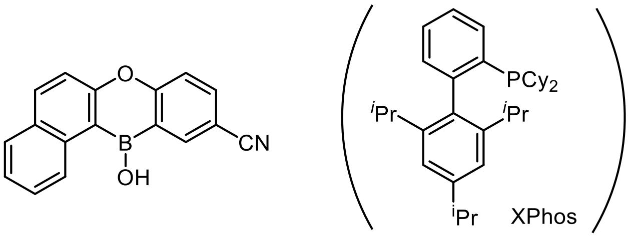
^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 105.2, 116.2 (d, J = 21 Hz), 118.8, 118.9, 119.8 (d, J = 7.6 Hz), 120.5, 121.4 (d, J = 25 Hz), 121.9, 136.0, 137.6, 156.5, 157.7 (d, J = 240 Hz), 162.6.

^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 35.9.

IR (ATR): 3445 w, 3086 w, 2358 w, 2339 w, 1885 w, 1806 w, 1609 m, 1558 w, 1488 m, 1451 s, 1386 s, 1297 s, 1265 m, 1213 m, 1186 s, 1172 m, 1132 m, 1111 s, 1084 s, 1004 w, 972 m, 900 m, 882 m, 867 m, 829 s, 815 s, 769 w, 751 m, 737 m, 689 m.

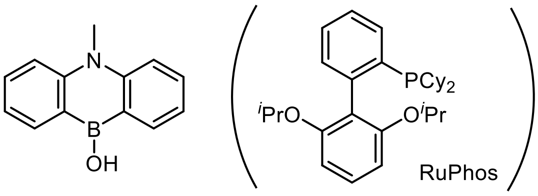
MS m/z (% relative intensity, CI): 241 (17), 240 (100), 239 (M^+, 31).
HRMS (CI): Calcd for $C_{13}H_{17}BFNO_2+H^+$ 240.0633, Found 240.0633.

12-Hydroxy-12*H*-benzo[*b*]naphtho[1,2-*e*][1,4]oxaborinine-10-carbonitrile (1p).



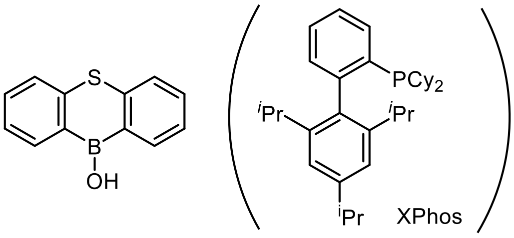
Method B was used. Instead of CyJohnPhos, XPhos was used as a ligand. R_f 0.20 (Hexane/EtOAc = 10/1). White solid (35 mg, 26%).
^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 7.53-7.57 (m, 1H), 7.60 (d, J = 8.7 Hz, 1H), 7.66-7.70 (m, 2H), 7.99 (d, J = 7.3 Hz, 1H), 8.09 (dd, J = 1.8, 8.7 Hz, 1H), 8.21 (d, J = 9.2 Hz, 1H), 8.87 (d, J = 2.3 Hz, 1H), 9.42 (d, J = 8.2 Hz, 1H), 10.4 (s, 1H).
^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 105.3, 114.3, 118.4, 118.8, 119.1, 121.5, 125.1, 127.6, 128.3, 128.6, 129.7, 135.0, 135.5, 136.1, 137.9, 160.9, 161.6.
^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 38.2.
IR (ATR): 3472 m, 3052 w, 2923 w, 2852 w, 2295 w, 1921 w, 1804 w, 1597 m, 1580 s, 1517 m, 1481 m, 1455 w, 1431 s, 1405 w, 1360 s, 1340 s, 1319 m, 1292 s, 1266 m, 1251 s, 1207 s, 1167 m, 1140 m, 1123 m, 1085 s, 1027 m, 966 s, 925 m, 903 m, 858 w, 829 m, 806 s, 782 m, 744 s, 714 s, 691 m, 664 m.
MS m/z (% relative intensity): 272 (20), 271 (M^+, 100), 270 (27), 243 (43).
HRMS (EI): Calcd for $C_{17}H_{10}BNO_2$ 271.0805, Found 271.0800.

5-Methyldibenzo[*b,e*][1,4]azaborinin-10(5*H*)-ol (1q). [CAS:123420-96-2]



Method B was used. Instead of CyJohnPhos, RuPhos was used as a ligand. R_f 0.17 (Hexane/EtOAc = 10/1). White solid (44 mg, 42%).
^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 3.79 (s, 3H), 7.11 (t, J = 7.4 Hz, 2H), 7.57 (d, J = 5.7 Hz, 2H), 7.61-7.66 (m, 2H), 8.22 (dd, J = 1.8, 5.9 Hz, 2H), 9.00 (s, 1H).
^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 35.0, 114.9, 118.6, 121.2, 132.0, 132.1, 148.3.
^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 38.0.
HRMS (EI): Calcd for $C_{13}H_{12}BNO$ 209.1012, Found 209.1011.
Spectroscopic data was in agreement with the reported values.[3e,22]

10*H*-Dibenzo[*b*,*e*][1,4]thiaborinin-10-ol (1r). [CAS: 1562266-28-7]



Method B was used. Instead of CyJohnPhos, XPhos was used as a ligand. R_f 0.20 (Hexane/EtOAc = 10/1). White solid (59 mg, 55%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 7.36-7.40 (m, 2H), 7.56-7.61 (m, 4H), 8.34-8.36 (m, 2H), 9.89 (s, 1H).

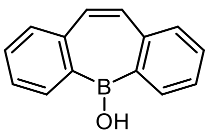
^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 124.6, 125.2, 129.4, 131.2, 133.8, 143.0.

^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 37.9.

HRMS (CI): Calcd for $C_{12}H_9BOS+H^+$ 213.0546, Found 213.0547.

Spectroscopic data was in agreement with the reported values.[23]

5*H*-Dibenzo[*b*,*f*]borepin-5-ol (1s). [CAS: 109476-11-1]



Method B was used. R_f 0.23 (Hexane/EtOAc = 10/1). White solid (228 mg, 37%).

^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 6.99 (s, 2H), 7.45-7.49 (m, 2H), 7.59-7.61 (m, 4H), 8.19 (d, *J* = 7.3 Hz, 2H), 9.86 (s, 1H).

^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 127.1, 130.7, 131.1, 131.8, 133.7, 136.9, 141.4.

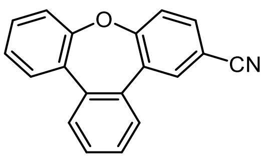
^{11}B NMR (DMSO-d_6, 128.27 MHz): δ 42.4.

IR (ATR): 3056 w, 3021 w, 2364 w, 1735 w, 1651 w, 1594 w, 1543 w, 1425 m, 1389 w, 1311 w, 1279 m, 1240 w, 1205 w, 1165 w, 1138 m, 1042 w, 962 w, 914 w, 886 w, 873 w, 842 m, 814 s, 768 m, 720 m.

MS m/z (% relative intensity, CI): 208 (10), 207 (55), 206 (M^+, 28), 193 (37).

HRMS (CI): Calcd for $C_{14}H_{11}BO+H^+$ 207.0982, Found 207.0979.

Tribenzo[*b*,*d*,*f*]oxepine-6-carbonitrile (6a).



R_f 0.29 (Hexane/EtOAc = 10/1). White solid (50 mg, 75%). Mp = 144 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.27-7.31 (m, 2H), 7.35-7.40 (m, 2H), 7.50-7.58 (m, 4H), 7.62-7.66 (m, 2H), 7.86 (d, *J* = 1.8 Hz, 1H).

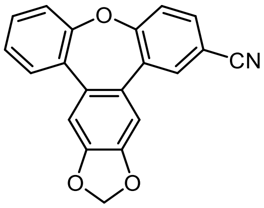
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 109.7, 118.6, 121.0, 122.4, 126.4, 128.7, 129.4, 129.6, 129.7, 129.9, 130.0, 132.4, 133.2, 134.0, 134.6, 134.7, 136.7, 159.4, 163.3.

IR (ATR): 3065 w, 2923 w, 2360 w, 2339 w, 1904 w, 1600 w, 1571 w, 1484 s, 1427 m, 1395 w, 1280 w, 1240 s, 1218 m, 1119 w, 1096 w, 1042 w, 939 w, 912 m, 889 w, 864 m, 843 m, 825 m, 789 m, 768 m, 734 s, 719 m, 690 w.

MS m/z (% relative intensity): 270 (21), 269 (M^+, 100), 241 (38), 240 (56), 238 (11), 107 (27), 94 (10).

HRMS (EI): Calcd for $C_{19}H_{11}NO$ 269.0841, Found 269.0838.

[1,3]Dioxolo[4',5':4,5]benzo[1,2-*d*]benzo[*b*]benzo[*f*]oxepine-6-carbonitrile (6b).



The reaction time was 48 h. R_f 0.14 (Hexane/EtOAc = 10/1). White solid (53 mg, 68%). Mp = 226 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 6.08 (s, 1H), 6.09 (s, 1H), 7.01 (s, 1H), 7.09 (s, 1H), 7.24-7.28 (m, 2H), 7.32-7.37 (m, 2H), 7.47 (dd, *J* = 1.4, 7.8 Hz, 1H), 7.60 (dd, *J* = 2.3, 8.5 Hz, 1H), 7.76 (d, *J* = 2.3 Hz, 1H).

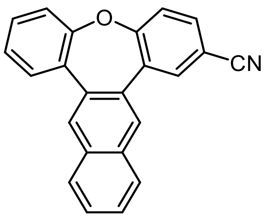
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 102.4, 109.6, 109.9, 110.1, 119.0, 121.4, 122.8, 126.8, 129.0, 130.0, 130.2, 131.6, 132.7, 133.3, 134.1. 134.9, 148.7, 149.2, 159.2, 163.1.

IR (ATR): 3078 w, 1920 w, 2358 w, 1625 w, 1574 w, 1507 m, 1485 s, 1449 m, 1415 m, 1392 w, 1368 w, 1264 m, 1247 m, 1224 s, 1199 w, 1165 w, 1119 w, 1040 m, 930 m, 869 m, 734 m, 818 w, 782 w, 765 w, 741 m, 672 w.

MS m/z (% relative intensity): 314 (22), 313 (M^+, 100), 254 (16), 227 (14).

HRMS (EI): Calcd for $C_{20}H_{11}NO_3$ 313.0739, Found 313.0741.

Dibenzo[*b,f*]naphtho[2,3-*d*]oxepine-7-carbonitrile (6c).



The reaction time was 48 h. R_f 0.23 (Hexane/EtOAc = 10/1). White solid (57 mg, 71%). Mp = 225 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.31-7.34 (m, 2H), 7.37-7.42 (m, 2H), 7.55-7.59 (m, 2H), 7.62-7.65 (m, 1H), 7.72 (d, *J* = 6.8 Hz, 1H), 7.93-7.96 (m, 2H), 8.00-8.02 (m, 2H), 8.08 (s, 1H).

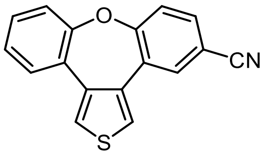
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 109.8, 118.6, 121.1, 122.4, 126.5, 127.2, 127.4, 128.1, 128.2, 129.0, 129.2, 129.8, 130.4, 132.5, 132.6, 132.9, 133.1, 133.4, 134.2, 134.3, 134.8, 159.5, 163.5.

IR (ATR): 3053 w, 1600 w, 1572 w, 1483 m, 1436 w, 1399 w, 1333 w, 1281 w, 1234 m, 1190 m, 1119 w, 1102 w, 1038 w, 1014 w, 982 w, 950 w, 917 w, 901 m, 888 m, 848 m, 822 m, 781 m, 749 s, 697 w.

MS m/z (% relative intensity): 320 (26), 319 (M^+, 100), 291 (14), 290 (31), 288 (11).

HRMS (EI): Calcd for $C_{23}H_{13}NO$ 319.0997, Found 319.0995.

Dibenzo[*b,f*]thieno[3,4-*d*]oxepine-5-carbonitrile (6d).



The reaction time was 48 h. R_f 0.23 (Hexane/EtOAc = 10/1). White solid (34 mg, 50%). Mp = 148 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.23-7.27 (m, 1H), 7.23-7.37 (m, 2H), 7.40 (d, *J* = 8.7 Hz, 1H), 7.57-7.62 (m, 4H), 7.87 (d, *J* = 2.3 Hz, 1H).

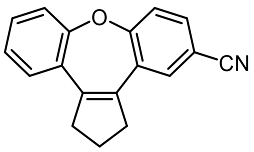
^{13}C NMR ($CDCl_3$, 150.92 MHz): δ 109.6, 118.5, 121.8, 123.2, 123.5, 124.4, 126.3, 128.3, 129.1, 129.7, 130.5, 133.0, 133.1, 135.7, 137.3, 156.2, 160.1.

IR (ATR): 3098 w, 1578 w, 1533 w, 1501 w, 1469 m, 1455 m, 1246 s, 1209 m, 1190 m, 1168 w, 1122 w, 1102 w, 1034 w, 947 w, 904 w, 881 w, 850 m, 827 w, 800 m, 780 m, 749 m, 722 w, 708 w.

MS m/z (% relative intensity): 276 (20), 275 (M^+, 100), 247 (14), 246 (33), 137 (13).

HRMS (EI): Calcd for $C_{17}H_9NOS$ 275.0405, Found 275.0403.

2,3-Dihydro-1*H*-dibenzo[*b,f*]cyclopenta[*d*]oxepine-5-carbonitrile (6e).



The reaction time was 48 h. R_f 0.31 (Hexane/EtOAc = 10/1). White solid (45 mg, 70%). Mp = 153 °C.

^{1}H NMR ($CDCl_3$, 399.78 MH.z): δ 2.16 (quint, *J* = 7.8 Hz, 2H), 2.89-2.98 (m, 4H), 7.15-7.33 (m, 5H), 7.47 (d, *J* = 1.8 Hz, 1H), 7.54 (dd, *J* = 3.1, 8.2 Hz, 1H).

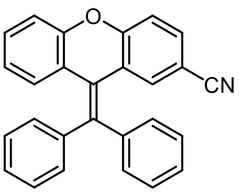
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 22.4, 36.0, 36.2, 108.9, 118.8, 121.2, 122.4, 125.6, 127.0, 130.0, 130.1, 130.8, 132.3, 132.9, 136.0, 140.5, 155.6, 159.5.

IR (ATR): 2958 w, 2844 w, 1617 w, 1566 w, 1483 s, 1442 m, 1398 w, 1296 w, 1265 m, 1225 s, 1188 w, 1134 m, 1116 w, 1061 w, 944 w, 880 m, 844 m, 780 s, 756 s, 685 w..

MS m/z (% relative intensity): 260 (19), 259 (M^+, 100), 258 (26), 245 (13), 244 (73), 243 (42), 231 (10), 230 (21).

HRMS (EI): Calcd for $C_{18}H_{13}NO$ 259.0997, Found 259.0994.

9-(Diphenylmethylene)-9*H*-xanthene-2-carbonitrile (6f).



The reaction time was 48 h. R_f 0.31 (Hexane/EtOAc = 10/1). Pale yellow solid (68 mg, 73%). Mp = 208 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 6.71-6.78 (m, 1H), 6.89 (d, *J* = 8.2 Hz, 1H), 7.13-7.20 (m, 4H), 7.21-7.34 (m, 10H), 7.37 (dd, *J* = 1.8, 8.7 Hz, 1H).

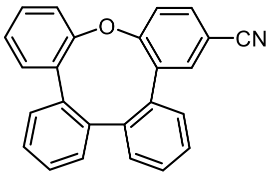
^{13}C NMR ($CDCl_3$, 159.92 MHz): δ 106.0, 116.5, 117.7, 118.7, 123.4, 123.6, 123.7, 125.6, 127.3, 127.8, 128.6, 128.8 (2C), 129.0 (2C), 129.2 (5C), 131.6, 133.7, 141.2, 142.0, 142.3, 153.0, 156.7.

IR (ATR): 3074 w, 1595 w, 1489 w, 1470 m, 1448 m, 1415 w, 1297 w, 1255 s, 1199 w, 1172 w, 1155 w, 1134 w, 1105 w, 1074 w, 1031 w, 1000 w, 946 w, 900 w, 875 w, 847 w, 827 m, 799 w, 764 m, 745 s, 703 s.

MS m/z (% relative intensity): 372 (29), 371 (M^+, 100), 370 (18), 293 (20).

HRMS (EI): Calcd for $C_{27}H_{17}NO$ 371.1310, Found 371.1310.

Tetrabenzo[*b,d,f,h*]oxonine-6-carbonitrile (6g).



The reaction time was 48 h. R_f 0.29 (Hexane/EtOAc = 10/1). White solid (58 mg, 67%). Mp = 171 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 6.87-6.94 (m, 4H), 6.98 (d, *J* = 8.7 Hz, 1H), 7.06-7.12 (m, 3H), 7.14-7.23 (m, 3H), 7.24-7.27 (m, 1H), 7.29-7.32 (m, 2H), 7.39 (dd, *J* = 2.3, 8.7 Hz, 1H).

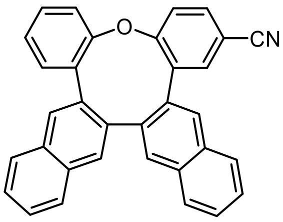
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 105.6, 118.9, 120.4, 121.1, 124.3, 127.5, 127.6, 127.7, 127,8, 127.9, 128.0, 128.5, 128.9, 129.0, 130.8, 131.3, 132.5, 133.1, 136.3, 137.6, 138.0, 141.6, 141.7, 152.5, 157.2.

IR (ATR): 3065 w, 1600 w, 1566 w, 1488 w, 1466 m, 1432 w, 1391 w, 1311 w, 1282 m, 1242 m, 1187 w, 1159 w, 1132 w, 1105 w, 1056 w, 1006 w, 942 w, 893 w, 852 w, 837 w, 750 s, 687 w.

MS m/z (% relative intensity): 346 (25), 345 (M^+, 100), 344 (51), 330 (14), 329 (14), 328 (57), 327 (26), 326 (18), 325 (12), 314 (17), 144 (15).

HRMS (EI): Calcd for $C_{25}H_{15}NO$ 345.1154, Found 345.1151.

Dibenzo[*b,h*]dinaphtho[2,3-*d*:2',3'-*f*]oxonine-7-carbonitrile (6h).



The reaction time was 48 h. R_f 0.46 (Hexane/EtOAc = 20/1). White solid (57 mg, 51%). Mp = 214 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 6.62-6.66 (m, 1H), 6.73 (dd, *J* = 1.8, 7.3 Hz, 1H), 6.86 (d, *J* = 8.2 HZ, 1H), 6.92 (d, *J* = 8.7 Hz, 1H), 6.96-7.00 (m, 2H), 7.07 (d, *J* = 8.2 Hz, 1H), 7.20-7.22 (m, 2H), 7.24-7.25 (m, 1H), 7.26-7.28 (m, 1H), 7.31 (d, *J* = 8.7 Hz, 1H), 7.38-7.45 (m, 2H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.77 (dd, *J* = 2.7, 8.7 Hz, 2H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H).

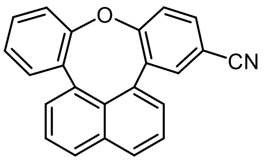
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 105.0, 118.8, 120.2, 120.9, 123.8, 125.8, 126.1, 126.2, 126.3, 126.4, 126.7, 126.8, 127.1, 128.0, 128.2, 128.4, 129.0, 129.9, 130.4, 131.6, 131.9, 132.5, 132.7, 132.8, 133.3, 134.3, 136.1, 136.3, 136.6, 136.7, 152.3, 157.2. One carbon peak is overlapped.

IR (ATR): 3056 w, 2924 w, 2853 w, 2359 w, 1679 w, 1599 w, 1566 w, 1481 m, 1460 w, 1437 w, 1393 w, 1308 m, 1281 m, 1242 m, 1184 w, 1130 w, 1067 w, 1037 w, 1020 w, 948 w, 898 w, 868 w, 833 w, 818 s, 752 s, 898 m.

MS m/z (% relative intensity, CI): 448 (20), 447 (36), 446 (100).

HRMS (CI): Calcd for $C_{33}H_{19}NO+H^+$ 446.1546, Found 446.1544.

Dibenzo[*b*,*g*]naphtho[1,8-*de*]oxocine-2-carbonitrile (6i).



The reaction time was 48 h. R_f 0.22 (Hexane/EtOAc = 40/1). White solid (38 mg, 48%). Mp = 157 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 7.21-7.32 (m, 4H), 7.34-7.36 (m, 2H), 7.52-7.59 (m, 4H), 7.81 (d, *J* = 2.3 Hz, 1H), 7.97 (dd, *J* = 1.4, 8.3 Hz, 1H), 8.00 (dd, *J* = 1.4, 8.3 Hz, 1H).

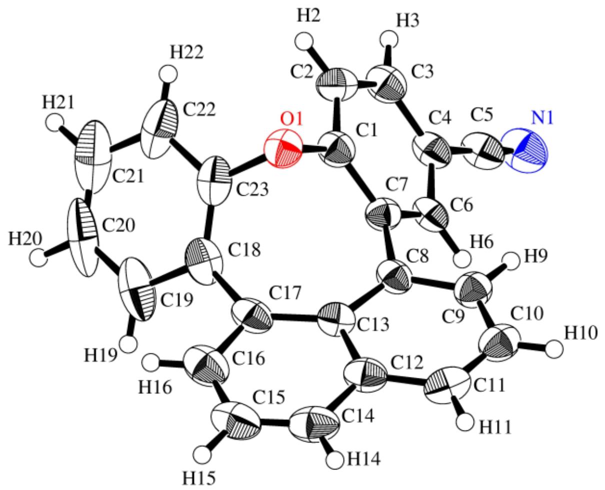
^{13}C NMR (CD_2Cl_2, 100.53 MHz): δ 110.5, 118.7, 122.0, 123.5, 125.9, 126.1, 127.0, 130.4, 130.8, 131.7, 132.3, 133.8, 133.9, 134.6, 135.5, 135.6, 135.7, 136.2, 136.5, 137.5, 138.8, 159.8, 164.0.

IR (ATR): 3060 w, 2923 w, 2853 w, 1600 w, 1569 w, 1478 m, 1442 w, 1396 w, 1363 w, 1322 w, 1263 w, 1243 w, 1207 w, 1184 m, 1130 w, 1107 w, 1054 w, 987 w, 913w, 876 w, 861 w, 843 w, 829 m, 808 w, 789 m, 768 s, 755 m, 734 w, 701 w.

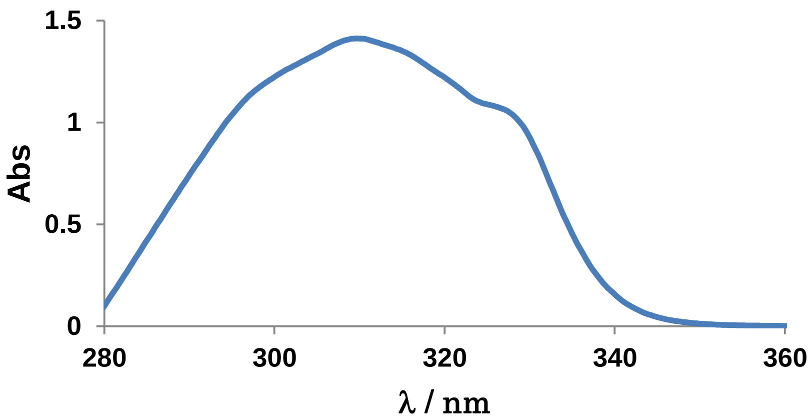
MS m/z (% relative intensity, CI): 322 (14), 321 (27), 320 (100), 319 (M^+, 11).

HRMS (CI): Calcd for $C_{23}H_{14}NO+H^+$ 320.1076, Found 320.1076.

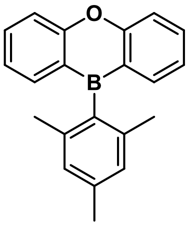
The solid-state structure was determined by X-ray crystallography.



UV vis absorption (λ_{max} = 310 nm) of **6i** in acetonitrile (*c* = 1.1 × 10^{-4} M) at room temperature.



10-Mesityl-10*H*-dibenzo[*b,e*][1,4]oxaborinine (7a).



R_f 0.34 (Hexane/CH_2Cl_2 = 20/1). White solid (47 mg, 53%). Mp = 163 °C.

^{1}H NMR (CD_2Cl_2, 399.78 MHz): δ 1.98 (s, 6H), 2.39 (s, 3H), 6.96 (s, 2H), 7.27 (t, *J* = 7.4 Hz, 2H), 7.63 (d, *J* = 8.7 Hz, 2H), 7.71 (d, *J* = 7.3 Hz, 2H), 7.75-7.79 (m, 2H).

^{13}C NMR (CD_2Cl_2, 100.53 MHz): δ 21.0, 22.6, 117.6, 122.5, 124.9, 127.0, 134.8, 136.2, 137.0, 138.6, 159.4. One of the B-aryl carbon signals cannot be observed.[14]

^{11}B NMR (CD_2Cl_2, 128.27 MHz): δ 56.4.

IR (ATR): 2908 w, 1602 m, 1576 m, 1475 w, 1449 w, 1430 s, 1375 w, 1329 m, 1307 m, 1258 m, 1214 m, 1155 m, 1130 w, 1098 w, 1029 w, 963 w, 908 w, 893 w, 872 w, 851 w, 780 w, 757 s, 725 w, 656 w.

MS m/z (% relative intensity): 299 (22), 298 (M^+, 100), 297 (31), 283 (13), 179 (15), 178 (11).

HRMS (EI): Calcd for $C_{21}H_{19}BO$ 298.1529, Found 298.1529.

2.5 References

(1) A special issue on organic electronics and optoelectronics using π-conjugated molecules edited by Forrest, S. R. and Thompson, M. E.: (a) *Chem. Rev.* **2007**, *107,* 923-1386. (b) Narita, A.; Wang, X.-Y.; Feng, X.; Müllen, K. *Chem. Soc. Rev.* **2015**, *44,* 6616. (c) Wu, J.; Pisula, W.; Müllen, K. *Chem. Rev.* **2007**, *107,* 718. (d) Sergeyev, S.; Pisula, W.; Greets, Y. H. *Chem Soc. Rev*. **2007**, *36*, 1902. (e) Laschat, S.; Baro, A.; Steinke, N.; Giesselmann, F.; Hägele, C.; Scalia, G.; Judele, R.; Kapatsina, E.; Sauer, S.; Schreivogel, A.; Tosoni, M. *Angew. Chem. Int. Ed.* **2007**, *46*, 4832. (f) Anthony, J. E. *Chem. Rev.* **2006**, *106,* 5028. (g) Bendikov, M.; Wudl, F.; Perepichka, D. F. *Chem. Rev.* **2004**, *104,* 489.

(2) A recent review on organodimetallic reagents: (a) Shimizu, M.; Hiyama, T. *Eur. J. Org. Chem.* **2013**, 8069. Selected examples. [Zr] (b) Takahashi, T.; Hara, R.; February, R. V. *J. Am. Chem. Soc.* **1996**, *118*, 5154. (c) Takahashi, T.; Li, Y.; Stepnicka, P.; Kitamura, M.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **2002**, *124*, 576. (d) Hilton, C. L.; Jamison, C. R.; King, B. T. *J. Am. Chem. Soc.* **2006**, *128*, 14824. (e) Hilton, C. L.; King, B. T. *Organometallics* **2006**, *25,* 4058. (f) Hilton, C. L.; Crowfoot, J. M.; Rempala, P.; King, B. T. *J. Am. Chem. Soc.* **2008**, *130*, 13392. (g) Zhou, L.; Nakajima, K.; Kanno, K.; Takahashi, T. *Tetrahedron Lett.* **2009**, *50*, 2722. [Sn] (h) Xue, X.; Scott, L. T. *Org. Lett.* **2007**, *9*, 3937. (i) Nagao, I.; Shimizu, M.; Hiyama, T. *Angew. Chem. Int. Ed.* **2009**, *48*, 7573. (j) Shimizu, M.; Nagao, I.; Kiyomoto, S.-i.; Hiyama, T. *Aust. J. Chem.* **2012**, *65,* 1277. (k) Kamimura, A.; Tanaka, T.; So, M.; Itaya, T.; Matsuda, K.; Kawamoto, T. *Org. Biomol. Chem.* **2016**, *14*, 8109. [B] (l) Goodby, J. W.; Hird, M.; Toyne, K. J.; Watson, T. *J. Chem. Soc., Chem. Commun.* **1994**, 1701. (m) Shimizu, M.; Shimono, K.; Kurahashi, T.; Kiyomoto, S.; Nagao, I.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 518. (n) Shimizu, M.; Nagao, I.; Tomioka, Y.; Hiyama, T. *Angew. Chem. Int. Ed.* **2008**, *47,* 8096. (o) Shimizu, M.; Tomioka, Y.; Nagao, I.; Hiyama, T. *Synlett* **2009**, *19*, 3147. (p) Shimizu, M.; Nagao, I.; Tomioka, Y.; Kadowaki, T.; Hiyama, T.

Tetrahedron **2011**, *67*, 8014. (q) Shimizu, M.; Tomioka, Y.; Nagao, I.; Kadowaki, T.; Hiyama, T. *Chem. Asian. J.* **2012**, *7*, 1644. (r) Kashihara, H.; Asada, T.; Kawashima, K. *Chem. Eur. J.* **2015**, *21*, 6523. (s) Shoji, Y.; Tanaka, N.; Muranaka, S.; Shigeno, N.; Sugiyama, H.; Takenouchi, K.; Hajjaj, F.; Fukushima, T. *Nat. Commun.* **2016**, *7*, 12704. see also [2j]. [Si]; (t) Ozaki, K.; Kawasumi, K.; Shibata, M.; Ito, H.; Itami, K. *Nat. Commun.* **2015**, *6*, 6251. see also (2a2) and (2b2). [Li] Recent reviews on organodilithium reagents. (u) Zhang, W.-X. ; Xi, Z. *Org. Chem. Front.* **2014**, *1*, 1132. (v) Zhang, S.; Zhang, W.-X.; Xi, Z. *Top. Organomet. Chem.* **2014**, *47*, 1. [Mg] (w) Wei, J.; Liu, L.; Zhan, M.; Xu, L.; Zhang, W.-X.; Xi, Z. *Angew. Chem. Int. Ed.* **2014**, *53*, 5634. (x) Fang, H.; Li, G.; Mao, G.; Xi, Z. *Chem. Eur. J.* **2004**, *10*, 3444. [Al] (y) Fang, H.; Zhao, C.; Li, G.; Xi, Z. *Tetrahedron* **2003**, *59*, 3779. [Fe] (z) Li, G.; Fang, H.; Li, Z.; Xi, Z. *Chin. J. Chem.* **2003**, *21*, 219. [Ge] (a2) Ozaki, K.; Murai, K.; Matsuoka, W.; Kawasumi, K.; Ito, H.; Itami, K. *Angew. Chem. Int. Ed.* **2017**, *56*, 1361. (b2) Ozaki, K.; Matsuoka, W.; Ito, H.; Itami, K. *Org. Lett.* **2017**, *19*, 1930.

(3) The first synthesis: (a) Davidson, J. M.; French, C. M. *J. Chem. Soc.* **1960**, 191. (b) Maitlis, P. M. *J. Chem. Soc.* **1961**, 425. The use as an organocatalyst: (c) Dimitrijević, E.; Taylor, M. S. *Chem. Sci.* **2013**, *4*, 3298. Typical synthesis: (d) Niu, L.; Yang, H.; Jiang, Y.; Fu, H. *Adv. Synth. Catal.* **2013**, *355*, 3625. The use in Suzuki-Miyaura reaction: (e) Dimitrijević, E.; Cusimano, M.; Taylor, M. S. *Org. Biomol. Chem.* **2014**, *12*, 1391. Representative works on dibenzoheteraborine ring systems: (f) Kranz, M.; Hampel, F.; Clark, T. *J. Chem. Soc., Chem. Commun.* **1992**, 1247. (g) Agou, T.; Kobayashi, J.; Kawashima, T. *Chem. Eur. J.* **2007**, *13*, 8051.

(4) (a) Haddenham, D.; Bailey, C. L.; Vu, C.; Nepomuceno, G.; Eagon, S.; Pasumansky, L.; Singaram, B. *Tetrahedron* **2011**, *67*, 576. (b) Marciasini, L.; Richy, N.; Vaultier, M.; Pucheault, M. *Chem. Commun.* **2012**, *48*, 1553. (c) Marciasini, L. D.; Richy, N.; Vaultier, M.; Pucheault, M. *Adv. Synth. Catal.* **2013**, *35*5, 1083. (d) Marciasini, L. D.; Vaultier, M.; Pucheault, M. *Tetrahedron Lett.* **2014**, *55*, 1702. (e) Guerrand, H. D. S.; Marciasini, L. D.; Gendrineau, T.; Pascu, O.; Marre, S.; Pinet, S.; Vaultier, M.; Aymonier, C.; Pucheault, M. *Tetrahedron* **2014**, *70*, 6156. (f) Guerrand, H. D. S.; Marciasini, L. D.; Jousseaume, M.; Vaultier, M.; Pucheault, M. *Chem. Eur. J.* **2014**, *20*, 5573. (g) Guerrand, H. D. S.; Vaultier, M.; Pinet, S.; Pucheault, M. *Adv. Synth. Catal.* **2015**, *357*, 1167.

(5) Wolfe, J. P.; Buckwald, S. L. *Angew. Chem. Int. Ed.* **1999**, *38*, 2413.

(6) Synthesis of an ethanolamine adduct of **1s**: (a) van Tamelen, E. E.; Brieger, G.; Untch, K. G. *Tetrahedron Lett.* **1960**, *8*, 14. Leading references on the chemistry of dibenzoborepin: (b) Mercier, L. G.; Piers, W. E.; Parvez, M. *Angew. Chem. Int. Ed*. **2009**, *48*, 6108. (c) Messersmith, R. E.; Siegler, M. A.; Taver, J. D. *J. Org. Chem.* **2016**, *81*, 5595.

(7) Marciasini, L.; Cacciuttolo, B.; Vaultier, M.; Pucheault, M. *Org. Lett.* **2015**, *17*, 3532.

(8) Lam, K. C.; Marder, T. B.; Lin, Z. *Organometallics* **2010**, *29*, 1849.

(9) (a) Claghorn, J.; Lesem, M. D. *Drug Res.* **1996**, *46*, 243. (b) Sperling, W.; Demling, J. *Drugs Today* **1997**, *33*, 95. (c) Zimmermann, K.; Waldmeier, P. C.; Tatton, W. G. *Pure Appl. Chem.* **1999**, *71*, 2039. (d) X-ray crystallography of tribenzo[*b*,*d*,*f*]oxepine: Dobelmann, L.; Parham, A. H.; Büsing, A.; Buchholz, H.; König, B. *RSC Adv.* **2014**, *4*, 60473.

(10) (a) Chung, M.-I.; Ko, H.-H.; Yen, M.-H.; Lin, C.-N.; Yang, S.-Z.; Tsao, L.-T.; Wang, J.-P. *Helv. Chim. Acta.* **2000**, *83*, 1200. (b) Ko, H.-H.; Lin, C.-N.; Yang, S.-Z. *Helv. Chim. Acta.* **2000**, *83*, 3000. (c) Ko,

H.-H.; Yang, S.-Z.; Lin, C.-N. *Tetrahedron Lett.* **2001**, *42*, 5269. (d) Lu, Y.-H.; Lin, C.-N.; Ko, H.-H.; Yang, S.-Z.; Tsao, L.-T.; Wang, J.-P. *Helv. Chim. Acta.* **2002**, *8*5, 1626. (e) Lu, Y.-H.; Lin, C.-N.; Ko, H.-H.; Yang, S.-Z.; Tsao, L.-T.; Wang, J.-P. *Helv. Chim. Acta.* **2003**, *86*, 2566.

(11) Shi, J.; Chang, N.; Li, C.; Mei, J.; Deng, C.; Luo, X.; Liu, Z.; Bo, Z.; Dong, Y. Q.; Tang, B. Z. *Chem. Comun.* **2012**, *48*, 10675.

(12) X-ray crystallography of tetrabenzo[*b*,*d*,*f*,*h*]oxonine: Ref (3e).

(13) (a) Escande, A.; Ingleson, M. J. *Chem. Commun.* **2015**, *51*, 6257. (b) Kobayashi, J.; Kato, K.; Agou, T.; Kawashima, T. *Chem. Asian J.* **2009**, *4*, 42.

(14) Xu, S.; Haeffner, F.; Li, B.; Zakharov, L. N.; Liu, S.-Y. *Angew. Chem. Int. Ed.* **2014**, *53*, 6795.

(15) Dahl, T.; Tornøe, C. W.; Bang-Andersen, B.; Nielsen, P.; Jørgensen, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 1726.

(16) Mercier, L. G.; Piers, W. E.; Parvez, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 6108.

(17) Tobisu, M.; Igarashi, T.; Chatani, N. *Beilstein J. Org. Chem.* **2016**, *12*, 654.

(18) Donovan, P. M.; Scott, L. T. *J. Am. Chem. Soc.* **2004**, *126*, 3108.

(19) Güell, I.; Ribas, X. *Eur. J. Org. Chem.* **2014**, 3188.

(20) Chang, V. H. T.; Corey, J. Y. *J. Organomet. Chem.* **1980**, *190*, 217.

(21) Baba, K.; Tobisu, M.; Chatani, N. *Org. Lett.* **2015**, *17*, 70.

(22) Kajiyama, K.; Yoshimune, M.; Nakamoto, M.; Matsukawa, S.; Kojima, S.; Akiba, K. *Org. Lett.* **2001**, *3*, 1873.

(23) Dimitrijević, E.; Taylor, M. S. *Chem. Sci.* **2013**, *4*, 3298.

Chapter 3

Nickel-Catalyzed Reductive Reaction of C-O Bonds in Anisole Derivatives Using Diisopropylaminoborane

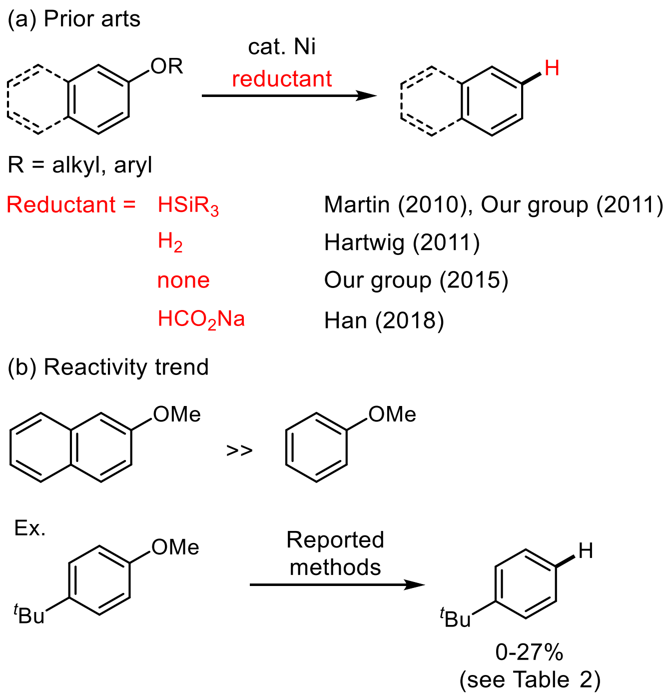
3.1 Introduction

Functional group removal reactions play a key role in organic synthesis, allowing electronic, steric and coordinating properties to enable characteristic conversion in a traceless manner. A methoxy group is one of common functionalities that exert a significant electronic effect to make it possible to activate aromatic rings toward S_EAr reactions with the regioselectivity at *ortho* and *para* positions.[1] Furthermore, a methoxy group can be utilized as an *ortho*-directing group in lithiation[2] and transition metal-catalyzed reactions,[3] as well as a *para*-directing group in other aromatic reactions.[4,5] Therefore, the removal reaction of a methoxy group is a valuable tool in organic chemistry.

Over the past decade, low valent Ni complexes were used in the cleavage reactions of C(aryl)-O bonds in inert phenol derivatives, including anisoles.[6] Meanwhile, several reductive cleavage of C(aryl)-O bonds in anisole derivatives were developed (**Scheme 1a**).[7,8] However, all of these reactions can only be applied to polyaromatic ethers such as naphthalene derivatives, and simple anisole derivatives cannot be used in these reactions (**Scheme 1b**).

Herein, the Ni-catalyzed reductive cleavage of C(aryl)-O bonds in anisole derivatives using diisopropylaminoborane **1a** was investigated. The development of this reaction enabled simple anisole derivatives to be reduced effectively.

Scheme 1. Ni-Catalyzed Reductive Cleavage of C-O Bonds in Anisole Derivatives



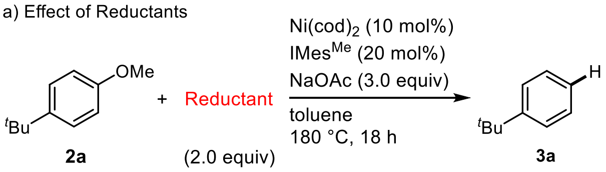
3.2 Results and Discussion

The author initially examined the effect of reductants on the reduction of 4-*tert*-butylanisole (**2a**) in the presence of Ni(cod)$_2$, IMes^{Me} and NaOAc (**Table 1a**). As previously reported, the addition of hydrosilane reagents (entries 1 and 2), which are effective reductants for the reductive deoxygenation of polycyclic aryl ethers,[7a,b] did not give the reduction product **3a**. The reaction also failed to proceed, when hydrogen was used as a reductant (entry 3)[7c]. The catalytic conditions in the absence of an external reductant[7d] afforded **3a** in only 11% yield (entry 4). The author next examined a series of boron-based reductants, expecting that substrate activated by the Lewis acidic boron atom would facilitate the difficult oxidative addition of C(aryl)-O bonds.[9] Reductive deoxygenation did not proceed when common utilized hydroboranes, such as HBcat (entry 5), 9-BBN (entry 6), HBpin (entry 7) and BH$_3$ (entry 8), were used. In contrast, using diisopropylaminoborane (**1a**) achieved the formation of **3a** in 79% yield (entry 9). The yield of **3a** was further improved to 93% by increasing the amount of **1a** to 2.5 equiv (entry 10). The use of excess **1a** was required for an efficient reaction in this reaction, because a significant amount of **1a** was consumed by undesired C(aryl)-H borylation of solvent toluene (ca. 55% based on **1a**). Although other solvents were explored to avoid C(aryl)-H borylation, such as 1,4-dioxane and ^{n}octane, using excess **1a** in toluene gave the highest yield of **3a**.

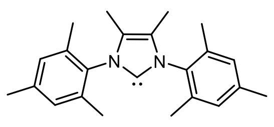
The author next turned my attention to investigating the effect of the ligand. Among the ligands reported to be effective for C(aryl)-O bond cleavage, IMes^{Me} was found to be the best ligand for reductive cleavage using **1a** (**Table 1b**). When the amount of IMes^{Me} was reduced to 10 mol%, the yield of **3a** decreased to 4% (entry 9). The yield of the reductive deoxygenation also decreased in the absence of NaOAc (entry 10).

Table 1. Optimization of Ni-Catalyzed Reductive Cleavage of **2a**

a) Effect of Reductants

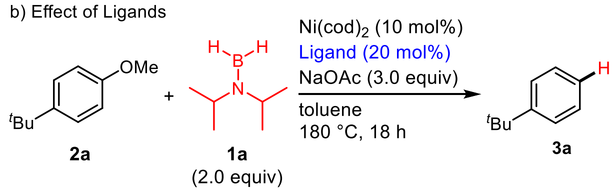


Entry	Reductant	GC yields (%)	
		3a	2a
1	HSiMe(OMe)$_2$	0	>99
2	HSiEt$_3$	0	95
3	H$_2$ (1 atm)	1	96
4	none	11	88
5	HBcat	0	98
6	9-BBN dimer	0	99
7	HBpin	13	85
8	BH$_3$•*i*Pr2NH	0	91
9	**1a**	79	17
10	**1a** (2.5 equiv)	93	6

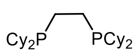


IMes^{Me}

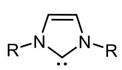
b) Effect of Ligands



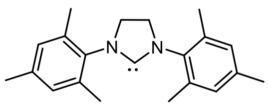
Entry	Ligand	GC yields (%)	
		3a	2a
1	PCy$_3$	0	75
2	PPh$_3$	0	92
3	dcype	0	>99
4	ICy	0	>99
5	IPr	36	64
6	IMes	0	58
7	SIMes	0	>99
8	IMes^{Me}	79	17
9	IMes^{Me} (10 mol%)	4	92
10	IMes^{Me} (without NaOAc)	51	7



dcype



ICy (R = cyclohexyl)
IPr (R = 2,6-^{i}Pr$_2$C$_6$H$_3$)
IMes (R = 2,4,6-Me$_3$C$_6$H$_2$)



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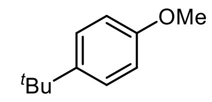
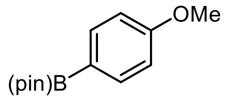
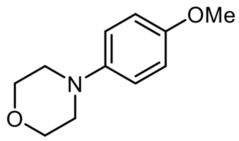
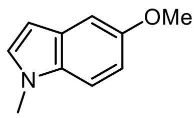
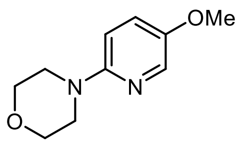
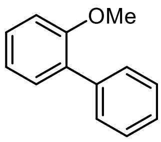
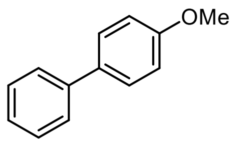
To evaluate the superiority of the catalytic system using **1a**, the reductive cleavage of several demanding substrates was performed under these conditions (Method A) and previously reported conditions (Methods B-D) (**Table 2**). Method B used $HSiMe(OMe)_2$ as reductant,[7b] Method C involved reduction under H_2 atmosphere in the presence of a stoichiometric amount of $AlMe_3$,[7c] and Method D represents the conditions in the absence of an external reductant.[7d] Anisole **2a**, which has no fused aromatic ring, did not undergo reductive cleavage reaction efficiently using Methods B-D, highlighting the outstanding effectiveness of Method A. Method A was advantageous in terms of functional group compatibility, as evidenced by the reductive cleavage of the anisole bearing a boryl group (**2b**). Methods C and D required more than a stoichiometric amount of NaO^{t}Bu, which limited their application to substrates bearing base-sensitive functional groups. In contrast, Method A allowed reductive cleavage to occur under virtually neutral conditions, which made the boryl group compatible. Electron-rich anisoles are among the most difficult substrates to reduce, and found to be ineffective at reducing this type of substrate (**2c**) with Methods B-D. Method A was able to reduce electron-rich anisoles successfully. Heteroaromatic substrates are another challenging class of compounds for which Methods B-D were also ineffective (**2d** and **2e**). For pyridine derivative **2e**, the pyridine ring was hydrogenated under a H_2 atmosphere (Method C). Substrates **2d** and **2e** were successfully reduced by Method A, demonstrating its robustness toward heteroaromatic systems. Furthermore, unlike other methods, Method A was uniquely tolerant of steric hindrance, as exemplified by the reaction of 2-methoxybiphenyl (**2f**). Method A performed better than reported methods, even in the case of relatively reactive biphenyl substrate **2g**, which underwent reductive cleavage at a low temperature of 60 °C, while Methods B-D did not form any desired product at this temperature.

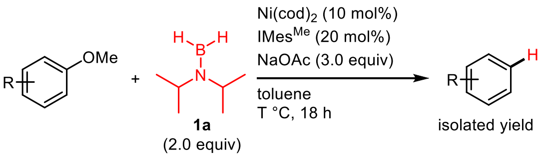
Table 2. Comparison with Reported Catalytic Methods[a]

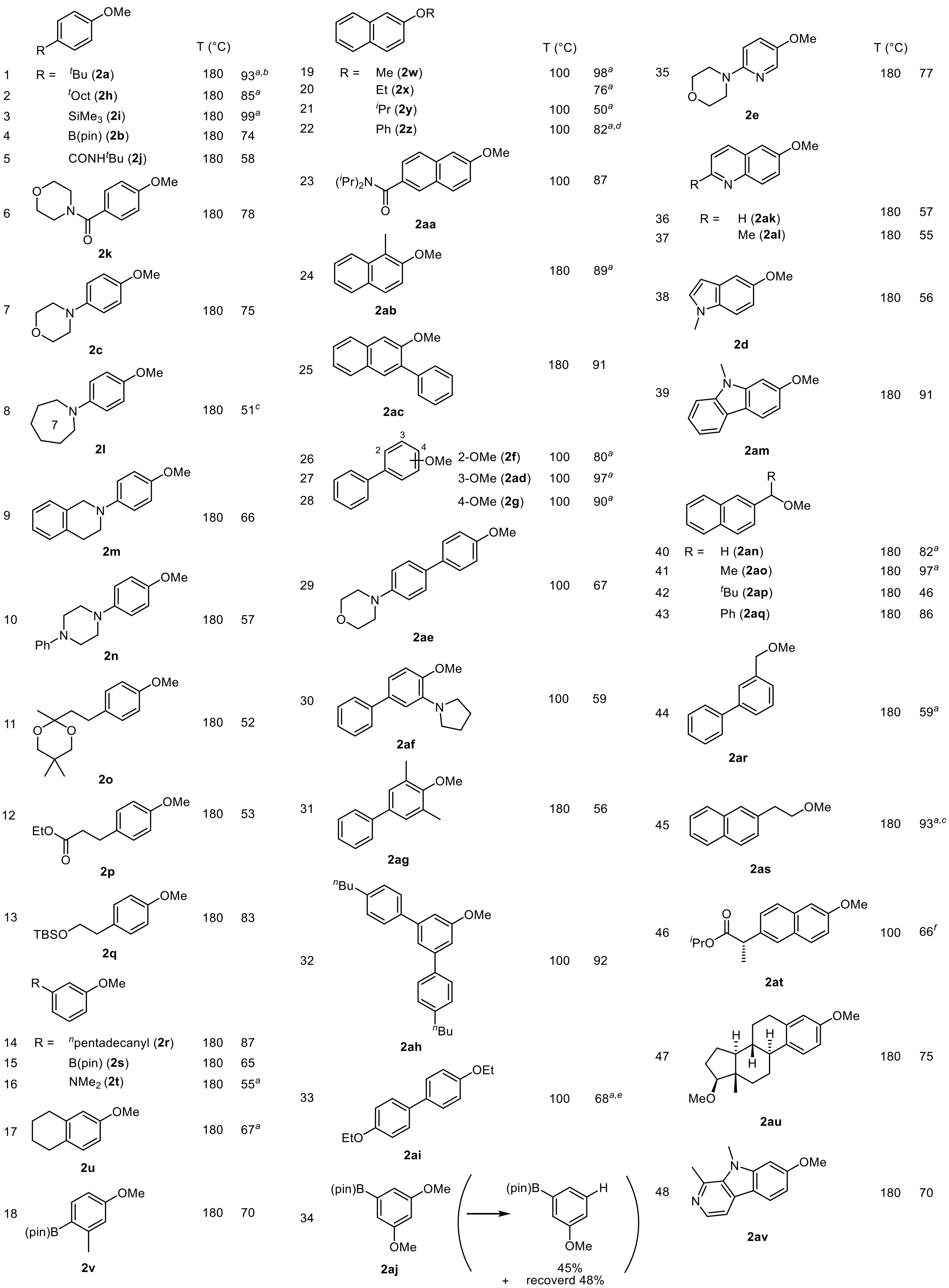
Substrate	Yield of reduced product [%] (yield of recovered substrate [%])				
	Method/	**A (This work)**	B	C	D
 **2a**		**93** (6)	1 (78)	13 (87)	27 (-)
 **2b**		**77** (0)	4 (96)	1 (1)	0 (6)
 **2c**		**77** (5)	0 (>99)	5 (89)	13 (37)
 **2d**		**56** (0)	3 (97)	0 (95)	24 (72)
 **2e**		**77** (0)	0 (>99)	0 (0)	0 (80)
 **2f**		**80** (16)	0 (>99)	0 (97)	13 (87)
 **2g**[b]		**88** (0)	0 (93)	0 (76)	0 (>99)

[a] Conditions: Method A: **1a** with Ni(cod)$_2$/IMes^{Me}/NaOAc; Method B: HSiMe(OMe)$_2$ with Ni(cod)$_2$/PCy$_3$[7b]; Method C: H_2 with Ni(cod)$_2$/SIPr/NaO^{t}Bu/AlMe$_3$[7c]; Method D: no external reductant with Ni(cod)$_2$/I(2-Ad)/NaO^{t}Bu[7d]. [b] Reactions were conducted at 60 °C.

Having established the exceptional reactivity of aminobororane **1a** in the reductive cleavage of aryl ethers (**Table 2**), the author next examined the scope of substrates in more detail (**Table 3**). The reaction was successfully applied to anisole derivatives bearing a series of functional groups, including silyl (**2i**), boryl (**2b**, **2s**, **2v**, **2aj**), ester (**2p**, **2at**), amide (**2j**, **2k**, **2aa**), and amino groups (**2c**, **2e**, **2l**, **2m**, **2n**, **2t**, **2ae, 2af**). In particular, the applicability of highly electron-rich *para*-amino-substituted anisoles (**2c, 2e, 2l-2n**) was notable. Although amide groups can be reduced by mild reducing agents in the presence of transition metal catalysts,[10] aryl ethers bearing both secondary (**2j**) and tertiary (**2k**, **2aa**) amides were compatible. Although ketones were reduced easily by **1a**, such substrates could be used by protecting as ketals (**2o**). Similarly, the incompatibility of hydroxyl groups was addressed by using the corresponding silyl ethers (**2q**). This reaction was also applied to naphthyl ethers (**2w-2ac**), which underwent reductive cleavage at 100 °C. Regarding the scope of alkoxy substituents, methoxy (**2w**), ethoxy (**2x**), isopropoxy (**2y**), and phenoxy (**2z**) groups were all cleaved under identical conditions. Biphenyl compounds (**2f**, **2g**, **2ad**) were also suitable substrates, undergoing reductive cleavage at 100 °C. Although the reductive cleavage of relatively reactive polyaromatic substrates were routinely performed at 100 °C, some reacted efficiently even at 60 °C (**2g** in **Table 2**). Methoxy groups located at sterically hindered positions, such as those in **2f, 2ac, 2af** and **2ag**, were reduced under these conditions to form corresponding reduction products. The tolerance of this catalytic method toward steric hindrance was further highlighted by the successful reduction of an anisole derivative bearing two *ortho* methyl groups (**2ag**). The reaction of 4,4'-diethoxy-1,1'-biphenyl (**2ai**) with 2.0 equiv of **1a** gave a mixture of biphenyl and 4-ethoxy-1,1'-biphenyl. Selective formation of 4-ethoxy-1,1'-biphenyl was difficult because 4-ethoxy-1,1'-biphenyl is less electron-rich, and therefore more reactive, than the starting **2ai**. The two ethoxy groups in **2ai** were completely cleaved by increasing the amount of **1a** to 3.0 equiv. In contrast, the selective removal of one of two methoxy groups was possible when less reactive 1,3-dimethoxybenzene derivative **2aj** was used. This reaction was also applicable to a variety of *N*-heteroaromatic compounds, including pyridines (**2e**), quinolines (**2ak**, **2al**), indoles (**2d**), and carbazoles (**2am**), which are common motifs in medicinal and materials chemistry. A methoxy group at the benzylic position can be reduced under these conditions, forming the corresponding alkylarenes. Furthermore, primary (**2an**, **2ar**) and secondary (**2ao-2aq**) benzylic ethers underwent reductive cleavage. A competition experiment between **2a** and 1-(*tert*-butyl)-4-(methoxymethyl)benzene (**2a'**) using 2.0 equiv of **1a** under the standard conditions led to the exclusive formation of **3a** with the complete recovery of **2a'**, indicating that C(benzyl)-O bonds are less reactive than C(aryl)-O bonds under these conditions (see the Experimental Section). Interestingly, the reaction of 2-(2-methoxyethyl)naphthalene (**2as**) under the standard reaction conditions afforded 2-ethylnaphthalene in 93% yield, demonstrating the potential utility of this method for the reductive cleavage of non-benzylic C(sp^3)-O bonds.[11] Similarly, 4-(2-methoxyethyl)-1,1'-biphenyl and (2-methoxyethyl)benzene can be applied to this reaction (see the Experimental Section). Methoxyarenes are common substructures found in various natural and unnatural biologically active compounds. Deoxygenated analogues of such compounds can readily be accessed using my protocol. For example, the removal of a methoxy group from naproxen (**2at**), estradiol (**2au**), and harmine (**2av**) derivatives was possible in one step under these Ni-catalyzed conditions using **1a**.

Table 3. Scope of the Substrates[a]



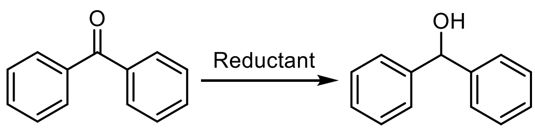


entry	substrate	T (°C)	yield (%)
1	R = ^{t}Bu (**2a**)	180	93[a,b]
2	^{t}Oct (**2h**)	180	85[a]
3	$SiMe_3$ (**2i**)	180	99[a]
4	B(pin) (**2b**)	180	74
5	CONH^{t}Bu (**2j**)	180	58
6	**2k**	180	78
7	**2c**	180	75
8	**2l**	180	51[c]
9	**2m**	180	66
10	**2n**	180	57
11	**2o**	180	52
12	**2p**	180	53
13	**2q**	180	83
14	R = ^{n}pentadecanyl (**2r**)	180	87
15	B(pin) (**2s**)	180	65
16	NMe_2 (**2t**)	180	55[a]
17	**2u**	180	67[a]
18	**2v**	180	70
19	R = Me (**2w**)	100	98[a]
20	Et (**2x**)		76[a]
21	^{i}Pr (**2y**)	100	50[a]
22	Ph (**2z**)	100	82[a,d]
23	**2aa**	100	87
24	**2ab**	180	89[a]
25	**2ac**	180	91
26	2-OMe (**2f**)	100	80[a]
27	3-OMe (**2ad**)	100	97[a]
28	4-OMe (**2g**)	100	90[a]
29	**2ae**	100	67
30	**2af**	100	59
31	**2ag**	180	56
32	**2ah**	100	92
33	**2ai**	100	68[a,e]
34	**2aj**		45% + recoverd 48%
35	**2e**	180	77
36	R = H (**2ak**)	180	57
37	Me (**2al**)	180	55
38	**2d**	180	56
39	**2am**	180	91
40	R = H (**2an**)	180	82[a]
41	Me (**2ao**)	180	97[a]
42	^{t}Bu (**2ap**)	180	46
43	Ph (**2aq**)	180	86
44	**2ar**	180	59[a]
45	**2as**	180	93[a,c]
46	**2at**	100	66[f]
47	**2au**	180	75
48	**2av**	180	70

[a] Yields determined by GC analysis owing to product volatility. [b] **1a** (0.75 mmol) was used. [c] Ni(cod)$_2$ (0.060 mmol) and IMes^{Me} (0.12 mmol) were used. [d] Phenol was obtained in 75% GC yield. [e] **1a** (0.90 mmol) was used. The yield refers to that for biphenyl. [f] NaOAc was not added.

To gain insight into the high reactivity of **1a** in this reductive cleavage of C(aryl)-O bonds, the reactivities of several common hydride reagents with **1a** in the reduction of benzophenone **4** were compared (**Table 4**). HSiMe(OMe)$_2$, HBcat and HBpin did not react with **4** in the absence of catalyst. In contrast, **1a** reduced **4** to give **5** in 76% yield at room temperature. This clearly indicated that the Lewis acidity of **1a** was higher than those of HSiMe(OMe)$_2$, HBcat, and HBpin, which allowed stronger interaction with the carbonyl oxygen atom of **4**, thereby facilitating the reduction.[12] The relatively high Lewis acidity of **1a** was further confirmed by ^{11}B NMR spectroscopy, which showed that the chemical shift of **1a** appeared down field of the others (**1a**, 35.5 ppm; HBcat, 28.7 ppm; HBpin, 28.3 ppm). Based on these results, the Lewis acid nature of **1a** probably played a key role in the reductive cleavage of aryl ethers. Although these observations indicated the relatively high Lewis acidity of **1a**, the author were unable to obtain any direct evidence of interaction between **1a** and aryl ether **2a** by ^{1}H and ^{11}B NMR, probably due to the equilibrium favoring their uncomplexed forms.

Table 4. Reduction of **4** by Using Hydrosilane or Hydroboranes[a]

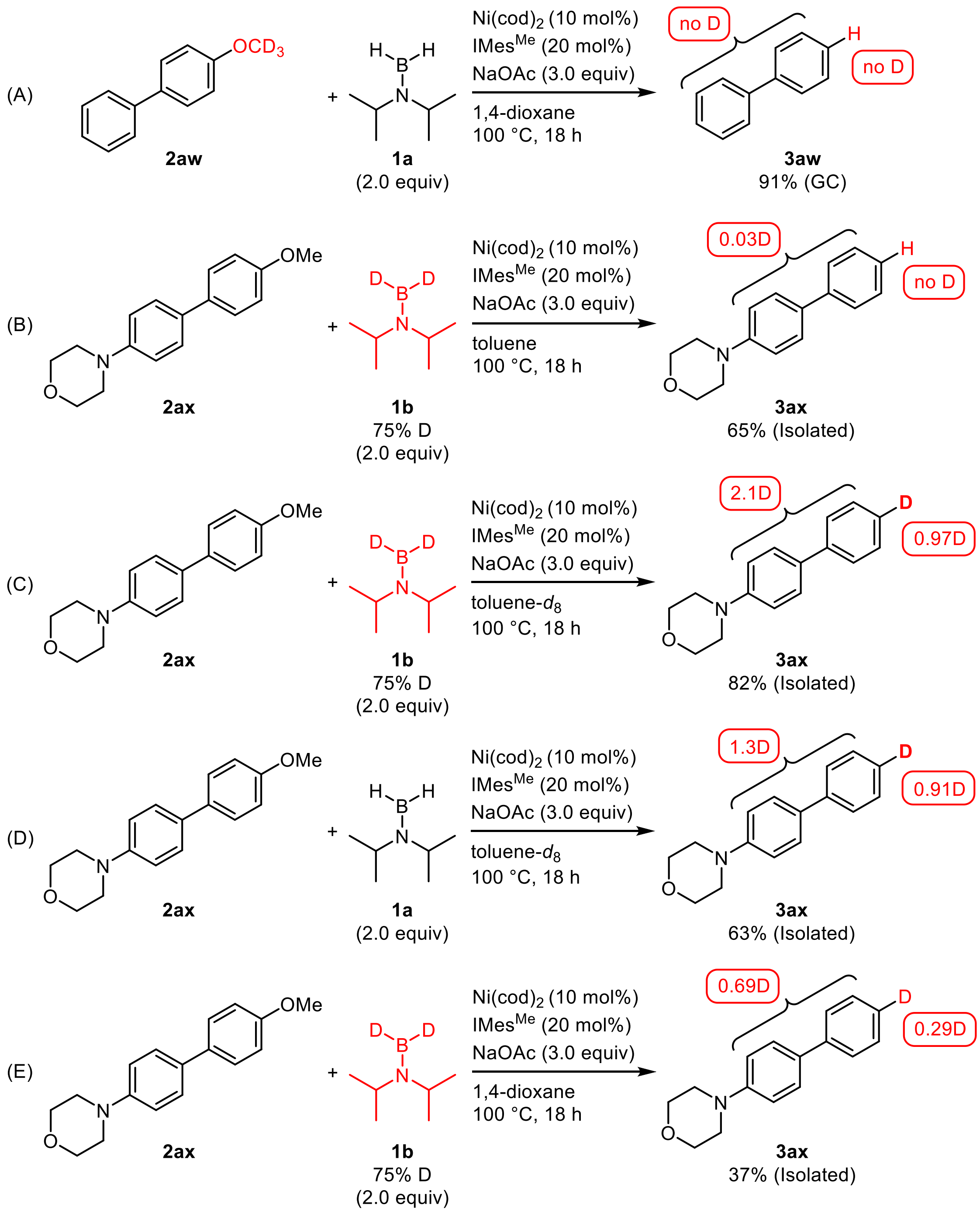


Reductant	Yield (%)[b]	δ (ppm)[c]
HSiMe(OMe)$_2$	0	-
HBcat	0	28.7
HBpin	0	28.3
1a	76	35.5

[a] Reaction conditions: **4** (0.30 mmol), hydrosilane or hydroborane (0.60 mmol), and THF (5.0 mL) at room temperature for 15 h. [b] Isolated yield is shown. [c] Chemical shifts in ^{11}B NMR using toluene-d_8.

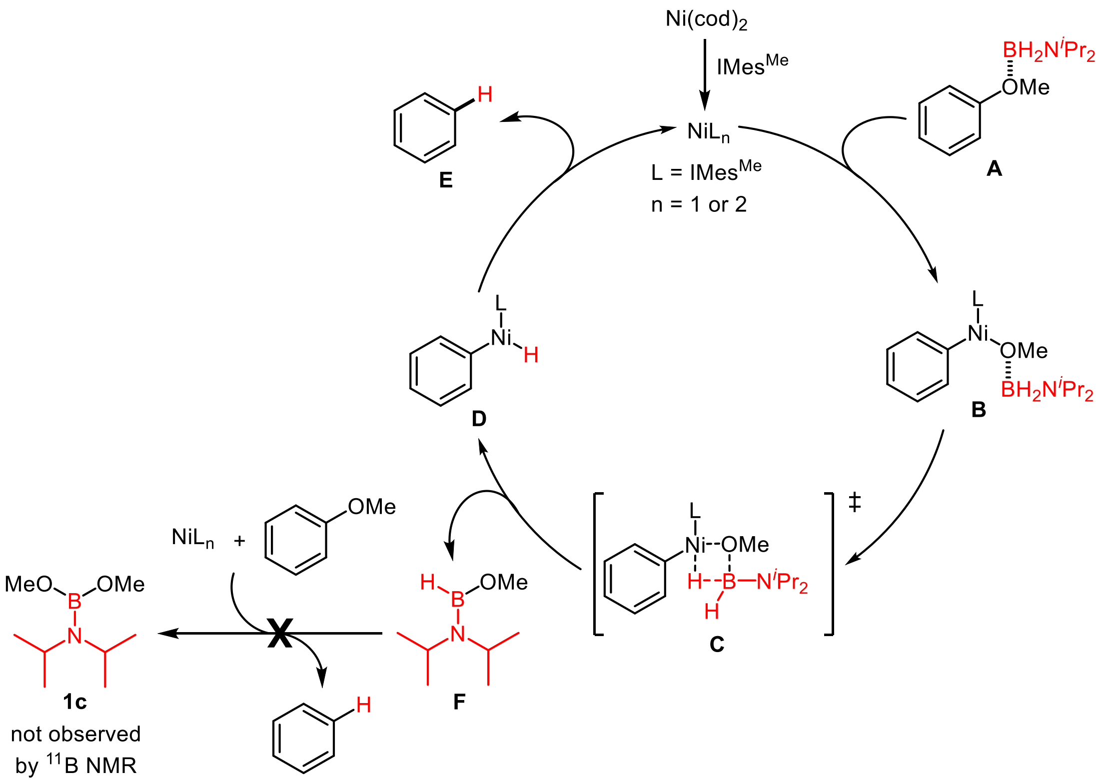
The author next conducted a series of deuterium labeling experiments to clarify the origin of hydride incorporated into the reduced product (**Scheme 2**). The Ni-catalyzed reaction of labeled substrate 4-CD$_3$O-biphenyl **2aw** with **1a** afforded deoxygenated product **3aw** without deuterium incorporation. This result indicated that, unlike the previously reported method,[7b] β-hydrogen elimination from the oxidative addition complex (Ar-Ni-OMe) was not a major pathway in this catalytic system (**Scheme 2A**). The author next conducted the reductive cleavage of **2ax** using a labeled aminoborane **1b** (75%D) and again found no deuterium incorporated into product **3ax** (**Scheme 2B**). In contrast, 97% deuterium was found to be incorporated at the *ipso* position of the product when the same reaction using **1b** was conducted in toluene-d_8 (**Scheme 2C**). Furthermore, 91% deuterium was incorporated into the product when the reaction of non-labelled **2ax** and **1a** was conducted in toluene-d_8 (**Scheme 2D**). These results indicated that an H/D exchange reaction was occurring between the reduced product and toluene solvent in the presence of **1a**.[13] Owing to this H/D exchange reaction, deuterium was also incorporated into other aromatic C-H bonds in **3ax** (**Scheme 2C**). To avoid H/D exchange with the solvent, we conducted the reaction of **2ax** with **1b** in 1,4-dioxane. However, H/D scrambling between the aromatic C-H bonds in **2ax** and **3ax** still hampered probing of the origin of incorporated hydride (**Scheme 2E**). Although rapid H/D exchange between **1b** and aromatic C-H bonds complicated the results of this labeling study, the source of hydride for the deoxygenation of C(aryl)-O bonds was most likely to be **1a**.

Scheme 2. Deuterium Labeling Experiments



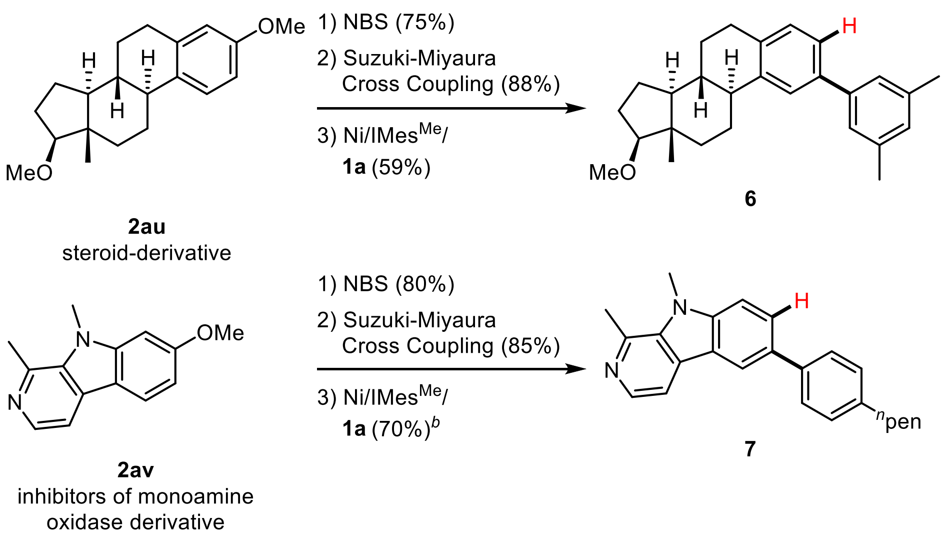
A possible mechanism is shown in **Scheme 3**. Given that using **1a** as the reducing agent is essential for the reaction to occur and that **1a** can reduce ketones in the absence of catalyst, coordination of the oxygen atom of anisole with the boron atom of **1a** to generate complex **A** was likely key for reductive cleavage. The formation of **A** should reduce the electron density of the C(aryl)-O bond of anisole, thereby facilitating oxidative addition of the C-O bond to $Ni(IMes^{Me})_n$ (n = 1 or 2) to form intermediate **B**. Subsequent hydride migration from boron atom to the Ni center, presumably occurring in an intramolecular manner through **C**, provides a Ni hydride **D**, which finally forms deoxygenated product **E** by reductive elimination accompanied by regeneration of the Ni catalyst. To investigate the fate of the boron residue, we analyzed the crude reaction mixture using ^{11}B NMR. Signals were observed at 38, 32, and 30 ppm in toluene-d_8. Dimethoxyaminoborane **1c** was not thought to be generated in this reaction, as the chemical shift corresponding to **1c** was confirmed to appear at 19 ppm by synthesizing **1c** separately. These results indicated that mono-hydride **F** was incapable of reducing anisole and that only one of the two B-H bonds in **1a** reacted in the deoxygenation reaction. Pathways involving Ni-hydride[14] or boryl Ni intermediate[15] cannot be completely excluded at this stage. However, these pathways require Ni(IV) or a dearomatized intermediate, which we currently believe to be unlikely. Several reductive cleavage reactions are proposed to proceed through heterogeneous catalysis, even though soluble metal complexes are used as catalyst precursors.[8,16] Therefore, we conducted a mercury test[17] for the Ni-catalyzed reaction of **2a** with **1a**. However, no significant decrease in the yield of **3a** was observed with the addition of mercury (79% without Hg vs 71% with Hg (23 equiv)), which suggested that this reaction was catalyzed by a homogeneous catalytic species.

Scheme 3. Proposed Mechanism



The potential utility of this reductive cleavage reaction of anisoles in the site-selective functionalization of biologically active phenol derivatives is demonstrated in **Scheme 4**. A methoxy group can activate an aromatic ring toward S_EAr and direct the reaction to occur at the *ortho* position. After serving as an activating group, a methoxy group can be removed using our method. Overall, a methoxy group can be used as a traceless *ortho*-directing group. This strategy allows C2 functionalization of steroidal architecture **2au** and regioselective functionalization of **2av**, a derivative of harmine (a reversible inhibitor of monoamine oxidase type-A).

Scheme 4. Synthetic Applications[a]



[a] Reaction Conditions: (1) NBS, CCl_4, rt. (2) cat. $Pd(P^tBu_3)_2$, Na_2CO_3, boryl compound, toluene/H_2O, reflux. (3) aryl ether (0.30 mmol), **1a** (0.60 mmol), $Ni(cod)_2$ (0.030 mmol), $IMes^{Me}$ (0.060 mmol), NaOAc (0.90 mmol), toluene (1.0 mL) at 180 °C for 18 h. [b] **1a** (1.2 mmol) was used.

3.3 Conclusion

In summary, the Ni-catalyzed reductive cleavage reaction of C(aryl)-O bonds in anisole derivatives using diisopropylaminoborane as a reductant has been developed. Unlike previously reported methods, this reaction can reduce simple anisole derivatives effectively, which is thought to depend on the higher Lewis acidity of diisopropylaminoborane than commonly used hydroborane reagents in catalytic reactions such as pinacolborane and catecholborane. The dramatically decreased reactivity of monoaromatic derivatives compared with polyaromatic derivatives is a common problem throughout the Ni-catalyzed cross-coupling reactions using inert aromatic electrophiles, including aryl fluorides, aryl amides, aryl esters and phenols.[6g] This study indicates that the use of high Lewis acidic reagents, which activate these substrates, helps solve this problem.

3.4 Experimental Section

3.4.1 General Information

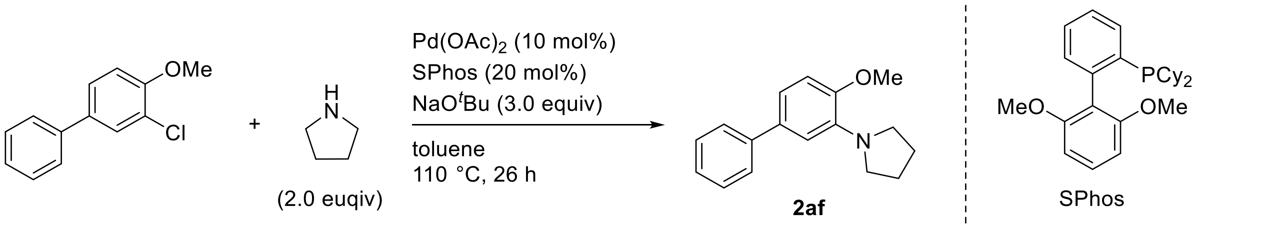
^1H NMR ^{13}C NMR and ^{11}B NMR spectra were recorded on a JEOL ECS-400 spectrometer or VARIAN UNITY

INOVA-600 spectrometer in $CDCl_3$ with tetramethylsilane as an internal reference standard, toluene-d_8 or benzene-d_6. Data are reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q= quartet, quin = quintet and m = multiplet), coupling constant (*J*) in Hz, and integration. Infrared spectra (IR) were obtained using a JASCO FT/IR-4200 spectrometer; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra and high resolution mass spectra (HRMS) were obtained on a JEOL JMS-700 spectrometer. Analytical gas chromatography (GC) was carried out on a Shimazu GC-2014 gas chromatograph, equipped with a flame ionization detector. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with SiO_2 (Silicycle Silica Flash F60 (230-400 mesh)) or NH Silica (Silica Gel 60 (sperical) NH_2 (40-50 μm)).

3.4.2 Materials

Ni(cod)$_2$ (Strem Chemicals), Pd(OAc)$_2$ (Wako), Pd(P^{t}Bu$_3$)$_2$ (TCI), PCy$_3$ (Aldrich), PPh$_3$ (Wako), dcype (Aldrich), IPr (TCI), HSiMe(OMe)$_2$ (TCI), HSiEt$_3$ (TCI), HBcat (Aldrich), 9-BBN dimer (Aldrich), HBpin (TCI), PCy$_3$ (Aldrich), PPh$_3$ (Wako), dcype (Aldrich), IPr (TCI), SPhos (TCI), CsF (TCI), DBU (TCI), NaOMe (Wako), LiOAc (Wako), NaOAc (Wako), KOAc (Wako), Na_2CO_3 (Nakalai tesque), $NaHCO_3$ (Nakarai tesque), Na_3PO_4 (Wako), K_2CO_3 (Nakarai tesque), toluene, super dehydrated (Wako), mesitylene (Wako), *p*-xylene (Wako), 1,4-dioxane, super dehydrated (Wako), *n*-octane (Wako), diglyme (Wako), MeOH, super dehydrated (Wako), THF, super dehydrated (Kanto kagaku), benzene-d_6 (Wako), toluene-d_8 (Euriso-top), **2a** (TCI), **2b** (TCI), **2f** (TCI), **2g** (TCI), **2s** (TCI), **2t** (TCI), **2u** (TCI), **2w** (TCI), **2x** (TCI), **2ad** (TCI), **2al** (TCI), **2ak** (TCI), **4** (TCI), pyrrolidine (TCI), Hg (Wako), 2-(3,5-dimethylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (TCI), NBS (Wako), CCl_4 (Wako), (4-pentylphenyl)boronic acid (TCI) and 2-phenylethyl methyl ether (TCI) were purchased from the commercial suppliers, and used as received. BH_3•^{i}Pr$_2$NH [CAS: 55124-35-1] and **1a** [CAS: 22092-92-8] was prepared according to the literature method.[18] **1b** was also synthesized by using $NaBD_4$ (Aldrich), instead of $NaBH_4$, according to the same literature method.[18] IMes^{Me} [CAS: 848085-28-9], IMes [CAS: 141556-42-5] and SIMes [CAS: 173035-11-5] were prepared from IMes^{Me}•HCl [CAS: 118916-80-5],[19] IMes•HCl (TCI) and SIMes•HCl (TCI) according to the literature procedure.[20] ICy [CAS: 181422-81-1] was prepared from ICy•HBF_4 (TCI) according to the literature procedure.[21] **2d** [CAS: 2521-13-3], **2h** [CAS: 5413-23-0], **2r** [CAS: 15071-57-5], **2al** [CAS: 1078-28-0], **2an** [CAS: 42101-58-7], **2ao** [CAS: 133339-20-5], **2ar** [CAS: 1016160-90-9], **2au** [CAS: 4945-14-7], 2-bromo-5-methoxypyridine [CAS: 105170-27-2], 4-bromo-4'-methoxy-1,1'-biphenyl [CAS: 58743-83-2] and 3-chloro-4-methoxy-1,1'-biphenyl [CAS: 21424-83-9] were prepared from 5-hydroxyindole (TCI), 4-(2,4,4-trimethylpentan-2-yl)phenol (TCI), 3-pentadecylphenol (TCI), 6-hydroxy-2-methylquinoline (TCI), 2-naphthalenemethanol (TCI), 1-(2-naphthyl)ethanol (TCI), 3-(hydroxymethyl)biphenyl (TCI), *β*-estradiol (TCI), 6-bromopyridin-3-ol (TCI), 4-bromo-4'-hydroxybiphenyl (TCI) and 2-chloro-4-phenylphenol (TCI) respectively, by the treatment with NaH (Wako) followed by MeI (TCI). **2e** [CAS: 1871740-78-1], **2l** [CAS: 120238-37-1], **2m** [CAS: 78317-83-6], **2n** [CAS: 15018-73-2] and **2ae** [CAS: 873949-97-4] were prepared by Buchwald-Hartwig cross-coupling reactions of 2-bromo-5-methoxypyridine [CAS: 105170-27-2], 4-bromoanisole (TCI) or 4-bromo-4'-methoxy-1,1'-biphenyl [CAS: 58743-83-2] used as a bromide, and morpholine (TCI), hexamethyleneimine (TCI),1,2,3,4-tetrahydroisoquinoline (TCI) or 1-phenylpiperazine (TCI) as an amine by the previously reported literature procedure.[22] **2q** [CAS: 1010078-75-7] was prepared from 4-methoxyphenethyl alcohol (TCI) by the protection with TBSCl (TCI). **2v** [CAS: 214360-68-6] and **2aj** [CAS: 365564-07-4] was prepared from 4-methoxy-2-methylphenylboronic acid (TCI) and 3,5-dimethoxyphenylboroni acid (TCI) by the protection with pinacol (TCI). **2c** [CAS: 27347-14-4],[23] **2i** [CAS: 877-68-9],[7d] **2j** [CAS: 19486-73-8],[24] **2k** [CAS: 7504-58-7],[25] **2o** [CAS: 500344-36-5],[26] **2y** [CAS: 15052-09-2],[27] **2z** [CAS: 19420-29-2],[28] **2aa** [CAS: 108711-00-8],[29] **2ab** [CAS: 3401-47-6],[30] **2ag** [CAS: 94001-39-5],[31] **2ah** [CAS: 1835666-41-5],[32] **2am** [CAS: 39027-93-5],[33] **2aq** [CAS: 130778-69-7],[34] **2at** [CAS: 156967-24-7][35] and **2aw** [CAS: 129603-22-1][36] were prepared by the previously reported literature procedure.

1-(4-Methoxy-[1,1'-biphenyl]-3-yl)pyrrolidine (2af).



$Pd(OAc)_2$ (31 mg, 0.14 mmol, 0.10 equiv), SPhos (113 mg, 0.28 mmol, 0.20 equiv), NaO^tBu (404 mg, 4.2 mmol, 3.0 equiv), toluene (3.0 mL), 3-chloro-4-methoxy-1,1'-biphenyl (300 mg, 1.4 mmol, 1.0 equiv) and pyrrolidine (196 mg, 2.8 mmol, 2.0 equiv) were added in a 20 mL-sample vial with a Teflon sealed screwcap, and then the suspension was stirred at 110 °C for 26 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The solvent was concentrated under reduced pressure, and purified by flash column chromatography over silica gel with hexane/EtOAc (20/1). The filtrate was concentrated in vacuo to give a pure product **2af** as a pale yellow solid (142 mg, 40%).

R_f 0.11 (hexane/EtOAc = 20/1). Mp = 69 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.95 (quin, J = 3.4 Hz, 4H), 3.35 (t, J = 6.4 Hz, 4H), 3.87 (s, 3H), 6.91 (d, J = 8.2 Hz, 1H), 7.00 (s, 1H), 7.05 (dd, J = 2.1, 8.2 Hz, 1H), 7.29 (tt, J = 1.1, 6.6 Hz, 1H), 7.38-7.42 (m, 2H), 7.55-7.58 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 24.8, 50.7, 55.8, 112.0, 114.7, 118.5, 126.6, 127.0, 128.7, 134.3, 139.8, 141.7, 150.1

IR (ATR): 2972 w, 2865 w, 2802 w, 2361 w, 1596 w, 1567 w, 1515 m, 1482 m, 1461 w, 1448 w, 1409 m, 1348 m, 1334 m, 1229 m, 1175 m, 1151 m, 1128 w, 1053 w, 1018 m, 971 w, 935 w, 880 w, 859, m, 816 m, 761 s, 700 m.

MS m/z (% relative intensity): 254 (14), 253 (M^+, 75), 252 (15), 239 (18), 238 (100).

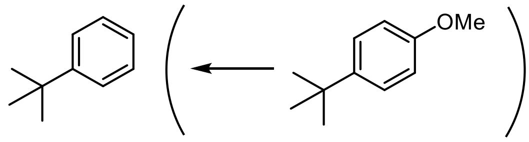
HRMS (EI): Calcd for $C_{17}H_{19}NO$ 253.1467, Found 253.1471.

3.4.3 General Procedures for the Ni-Catalyzed Reductive Reaction of C-O Bonds in Anisole Derivatives Using 1a

In a glovebox filled with nitrogen, $Ni(cod)_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), $IMes^{Me}$ (20 mg, 0.060 mmol, 0.20 equiv) and toluene (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv), an aryl alkyl ether (0.30 mmol, 1.0 equiv), and **1a** (68 mg, 0.60 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 100 or 180 °C for 18 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. The crude mixture was concentrated under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc solution. The filtrate was concentrated in vacuo to give a pure reduced product.

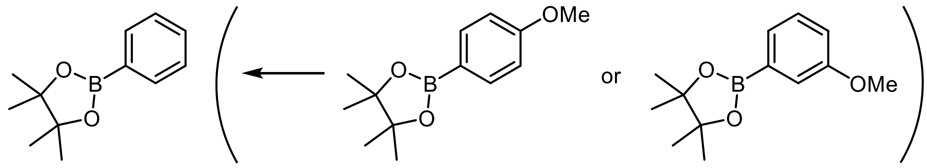
3.4.4 Spectroscopic Data for Products

***tert*-Butylbenzene (3a).** [CAS: 98-06-6]



The typical procedure was followed using **2a** except that 2.5 equiv of **1a** was added, and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (93%). The identity of **3a** was unambiguously confirmed by GC analysis using *tert*-butylbenzene (TCI) as an authentic sample.

4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaborolane (3b, 3s). [CAS: 24388-23-6]



The typical procedure was followed using **2b** or **2s**, and the reaction temperature was 180 °C. Isolated yields of the product from **2b** or **2s** were 74% or 65%, respectively.

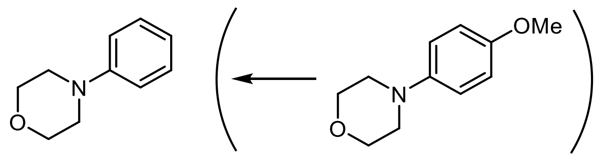
R_f 0.31 (hexane/EtOAc = 20/1). White solid (45 mg, 74% from **2b**), White solid (40 mg, 65% from **2s**).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.35 (s, 12H), 7.35-7.39 (m, 2H), 7.46 (tt, *J* = 1.4, 6.4 Hz, 1H), 7.80-7.82 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 25.0, 83.9, 127.9, 131.4, 134.9.

HRMS (EI): Calcd for $C_{12}H_{17}BO_2$ 204.1322, Found 204.1323.

4-Phenylmorpholine (3c). [CAS: 92-35-5]



The typical procedure was followed using **2c**, and the reaction temperature was 180 °C.

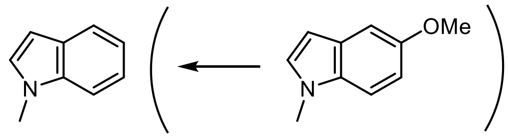
R_f 0.23 (hexane/EtOAc = 10/1). Pale yellow oil (37 mg, 75%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.15 (t, *J* = 4.8 Hz, 4H), 3.86 (t, *J* = 4.8 Hz, 4H), 6.87-6.94 (m, 3H), 7.26-7.31 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 49.5, 67.0, 115.8, 120.2, 129.3, 151.3.

HRMS (EI): Calcd for $C_{10}H_{13}NO$ 163.0997, Found 163.0997.

1-Methyl-1*H*-indole (3d). [CAS: 603-76-9]



The typical procedure was followed using **2d**, and the reaction temperature was 180 °C.

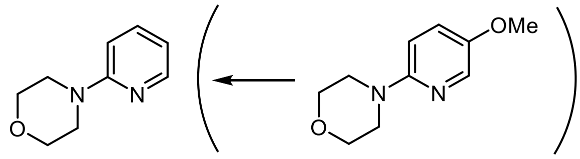
R_f 0.17 (hexane/EtOAc = 40/1). Colorless oil (22 mg, 56%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.78 (s, 3H), 6.48 (d, *J* = 3.2 Hz, 1H), 7.04 (d, *J* = 3.2 Hz, 1H), 7.08-7.12 (m, 1H), 7.20-7.24 (m, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 32.9, 101.0, 109.3, 119.4, 121.0, 121.6, 128.6, 128.9, 136.8.

HRMS (EI): Calcd for C_9H_9N 131.0735, Found 131.0732.

4-(Pyridin-2-yl)morpholine (3e). [CAS: 24255-25-2]



The typical procedure was followed using **2e**, and the reaction temperature was 180 °C.

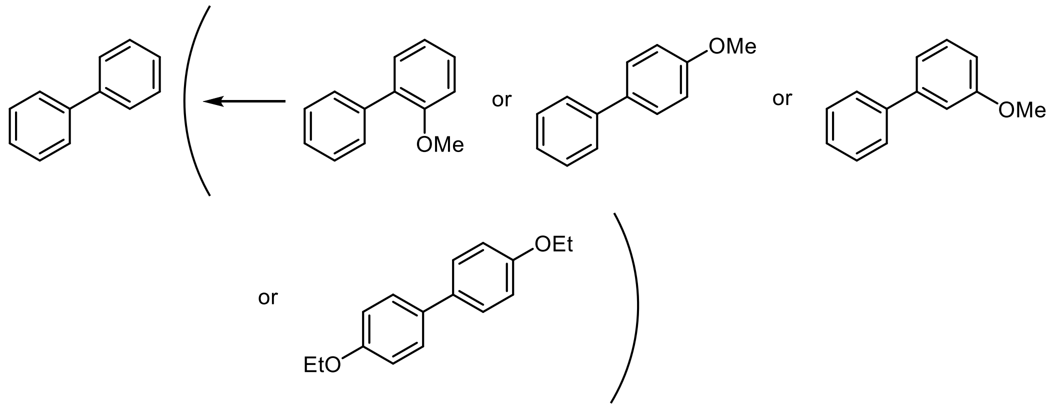
R_f 0.20 (NH silica, hexane/EtOAc = 20/1). Colorless oil (38 mg, 77%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.50 (t, *J* = 4.9 Hz, 4H), 3.83 (t, *J* = 4.9 Hz, 4H), 6.63-6.68 (m, 2H), 7.48-7.52 (m, 1H), 8.20-8.21 (m, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 45.7, 66.9, 107.1, 114.0, 137.7, 148.1, 159.7.

HRMS (EI): Calcd for $C_9H_{12}N_2O$ 164.0950, Found 164.0951.

Biphenyl (3f, 3g, 3ad, 3ai). [CAS: 92-52-4]



The typical procedure was followed using **2f**, **2g**, **2ad** or **2ai** except that 3.0 equiv of **1a** was added when using **2ai** as a substrate, and the reaction temperature was 100 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product. GC yields of a product from **2f**, **2g**, **2ad** or **2ai** were 80, 90, 97 or 68%, respectively.

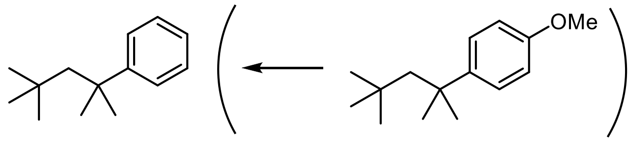
R_f 0.29 (hexane). White solid.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.35 (t, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.5 Hz, 4H), 7.60 (d, *J* = 7.5 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 127.3, 127.4, 128.9, 141.4.

HRMS (EI): Calcd for $C_{12}H_{10}$ 154.0783, Found 157.0785.

(2,4,4-Trimethylpentan-2-yl)benzene (3h). [CAS: 35293-37-9]



The typical procedure was followed using **2h**, and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (85%).

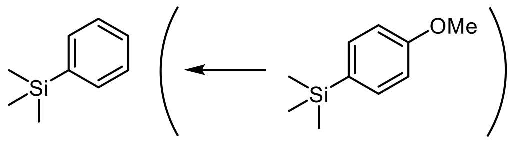
R_f 0.43 (hexane). Colorless oil.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.71 (s, 9H), 1.37 (s, 6H), 1.74 (s, 2H), 7.13-7.17 (m, 1H), 7.25-7.29 (m, 2H), 7.36-7.39 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 31.7, 31.9, 32.5, 38.7, 57.1, 125.3, 126.3, 127.9, 150.2.

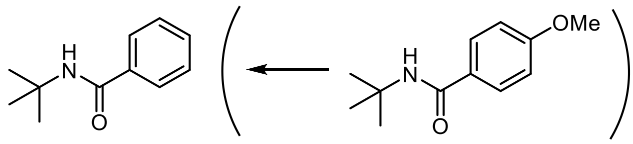
HRMS (EI): Calcd for $C_{14}H_{22}$ 190.1722, Found 190.1721.

Trimethyl(phenyl)silane (3i). [CAS: 768-32-1]



The typical procedure was followed using **2i**, and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (99%). The identity of **3i** was unambiguously confirmed by GC analysis using trimethyl(phenyl)silane (Aldrich) as an authentic sample.

***N*-(*tert*-Butyl)benzamide (3j).** [CAS: 5894-65-5]



The typical procedure was followed using **2j**, and the reaction temperature was 180 °C.

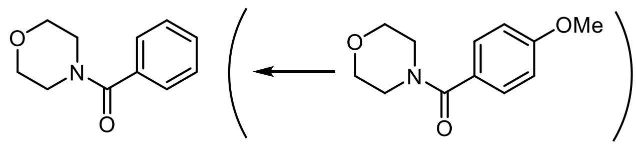
R_f 0.34 (hexane/EtOAc = 3/1). White solid (31 mg, 58%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.48 (s, 9H), 5.94 (br, 1H), 7.39-7.47 (m, 3H), 7.71-7.73 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 29.0, 51.8, 126.8, 128.6, 131.2, 136.1, 167.0.

HRMS (EI): Calcd for $C_{23}H_{32}N_2O_3$ 177.1154, Found 177.1153.

Morpholino(phenyl)methanone (3k). [CAS: 1468-28-6]



The typical procedure was followed using **2k**, and the reaction temperature was 180 °C.

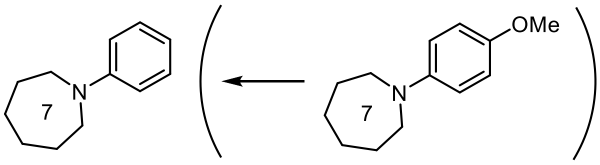
R_f 0.40 (hexane/EtOAc = 3/1). White solid (45 mg, 78%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.45-3.79 (m, 8H), 7.39-7.46 (m, 5H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 42.7 (br), 48.4 (br), 67.0, 127.2, 128.7, 130.0, 135.4, 170.6.

HRMS (CI): Calcd for $C_{11}H_{13}NO_2+H^+$ 192.1025, Found 192.1023.

1-Phenylazepane (3l). [CAS: 40832-99-3]



The typical procedure was followed using **2l** except that $Ni(cod)_2$ (20 mol%) and $IMes^{Me}$ (40 mol%) were used , and the reaction temperature was 180 °C.

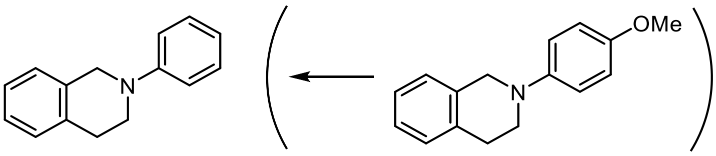
R_f 0.34 (hexane/EtOAc = 100/1). Colorless oil (27 mg, 51%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.50-1.56 (m, 4H), 1.77-1.78 (m, 4H), 3.45 (t, *J* = 6.0 Hz, 4H), 6.62 (t, *J* = 7.3 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 2H), 7.18-7.22 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 27.3, 27.9, 49.1, 111.2, 115.2, 129.4, 149.0.

HRMS (EI): Calcd for $C_{12}H_{17}N$ 175.1361, Found 175.1359.

2-Phenyl-1,2,3,4-tetrahydroisoquinoline (3m). [CAS: 3340-78-1]



The typical procedure was followed using **2m**, and the reaction temperature was 180 °C.

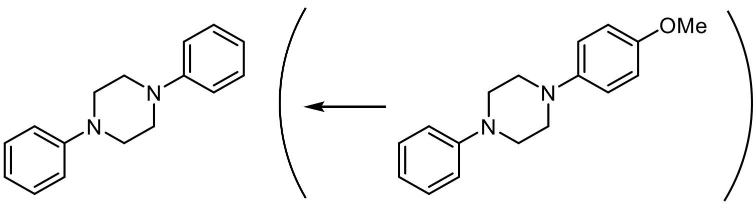
R_f 0.37 (hexane/EtOAc = 10/1). Pale yellow solid (41 mg, 66%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.98 (t, *J* = 5.9 Hz, 2H), 3.56 (t, *J* = 5.9 Hz, 2H), 4.41 (s, 2H), 6.83 (t, *J* = 7.3 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 2H), 7.14-7.21 (m, 4H), 7.26-7.31 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 29.2, 46.7, 50.8, 115.3, 118.8, 126.1, 126.5, 126.7, 128.6, 129.3, 134.5, 134.9, 150.6.

HRMS (EI): Calcd for $C_{15}H_{15}N$ 209.1204, Found 209.1203.

1,4-Diphenylpiperazine (3n). [CAS: 613-39-8]



The typical procedure was followed using **2n**, and the reaction temperature was 180 °C.

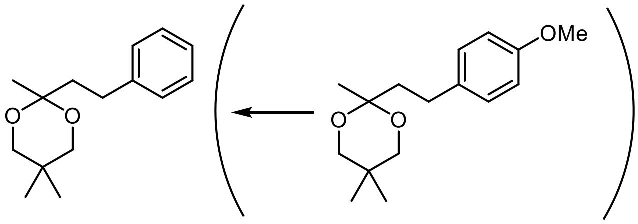
R_f 0.23 (hexane/EtOAc = 10/1). Pale yellow solid (41 mg, 57%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.35 (s, 8H), 6.90 (t, *J* = 7.3 Hz, 2H), 7.00 (d, *J* = 7.8 Hz, 4H), 7.28-7.32 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 49.6, 116.5, 120.3, 129.3, 151.3.

HRMS (EI): Calcd for $C_{16}H_{18}N_2$ 238.1470, Found 238.1471.

2,5,5-Trimethyl-2-phenethyl-1,3-dioxane (3o). [CAS: 92208-11-2]



The typical procedure was followed using **2o**, and the reaction temperature was 180 °C.

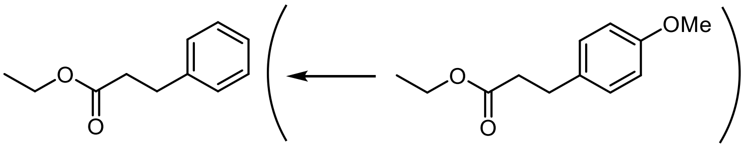
R_f 0.14 (hexane/EtOAc = 20/1). Pale yellow oil (37 mg, 52%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.93 (s, 3H), 1.04 (s, 3H), 1.44 (s, 3H), 1.98-2.03 (m, 2H), 2.74-2.79 (m, 2H), 3.49 (d, *J* = 11 Hz, 2H), 3.59 (d, *J* = 11 Hz, 2H), 7.18-7.24 (m, 3H), 7.27-7.31 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 20.9, 22.7, 22.9, 29.8, 30.1, 40.0, 70.5, 98.7, 125.8, 128.5, 142.6.

HRMS (EI): Calcd for $C_{15}H_{22}O_2$ 234.16207, Found 234.1617.

Ethyl 3-phenylpropanoate (3p). [CAS: 2021-28-5]



The typical procedure was followed using **2p**, and the reaction temperature was 180 °C.

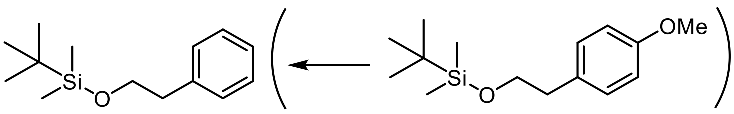
R_f 0.29 (hexane/EtOAc = 20/1). Colorless oil (28 mg, 53%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.24 (t, *J* = 6.9 Hz, 3H), 2.62 (t, *J* = 7.7 Hz, 2H), 2.95 (t, *J* = 7.7 Hz, 2H), 4.13 (q, *J* = 6.9 Hz, 2H), 7.19-7.22 (m, 3H), 7.27-7.32 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.4, 31.1, 36.1, 60.6, 126.4, 128.5, 128.6, 140.7, 173.1.

HRMS (EI): Calcd for $C_{11}H_{14}O_2$ 178.0994, Found 178.0994.

***tert*-Butyldimethyl(phenethoxy)silane (3q).** [CAS: 78926-09-7]



The typical procedure was followed using **2q**, and the reaction temperature was 180 °C.

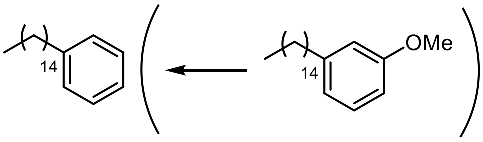
R_f 0.46 (hexane/EtOAc = 20/1). Colorless oil (59 mg, 83%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.00-0.001 (m, 6H), 0.89-0.90 (m, 9H), 2.84 (t, *J* = 7.4 Hz, 2H), 3.80-3.84 (m, 2H), 7.22-7.23 (m, 3H), 7.27-7.32 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ -5.3, 18.5, 26.1, 39.8, 64.7, 126.2, 128.3, 129.3, 139.3.

HRMS (CI): Calcd for $C_{14}H_{24}OSi+H^+$ 237.1675, Found 237.1678.

Pentadecylbenzene (3r). [CAS: 2131-18-2]



The typical procedure was followed using **2r**, and the reaction temperature was 180 °C.

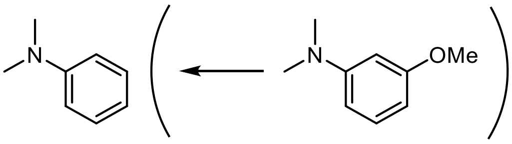
R_f 0.45 (hexane). Colorless oil (75 mg, 87%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.88 (t, *J* = 6.7 Hz, 3H), 1.25-1.30 (m, 24H), 1.51-1.64 (m, 2H), 2.59 (t, *J* = 7.3 Hz, 2H), 7.14-7.18 (m, 3H), 7.25-7.29 (m, 2H).

^{13}C NMR ($CDCl_3$, 150.92 MHz): δ 14.3, 22.9, 29.5, 29.6, 29.7, 29.8, 29.9, 31.7, 32.1, 36.2, 125.7, 128.3, 128.5, 143.1.

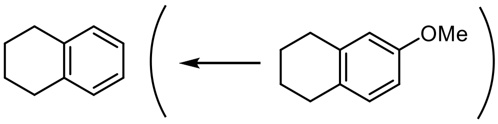
HRMS (EI): Calcd for $C_{21}H_{36}$ 288.2817, Found 288.2815.

***N*,*N*-Dimethylaniline (3t).** [CAS: 121-69-7]



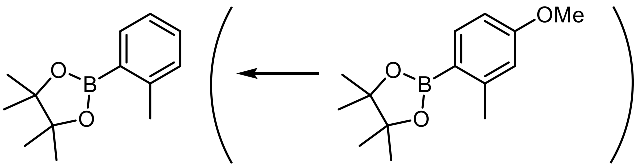
The typical procedure was followed using **2t**, and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (55%). The identity of **3t** was unambiguously confirmed by GC analysis using *N*,*N*-dimethylaniline (Wako) as an authentic sample.

1,2,3,4-Tetrahydronaphthalene (3u). [CAS: 119-64-2]



The typical procedure was followed using **2u**, and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (67%). The identity of **3u** was unambiguously confirmed by GC analysis using 1,2,3,4-tetrahydronaphthalene (TCI) as an authentic sample.

4,4,5,5-Tetramethyl-2-(*o*-tolyl)-1,3,2-dioxaborolane (3v). [CAS: 195062-59-0]



The typical procedure was followed using **2v**, and the reaction temperature was 180 °C.

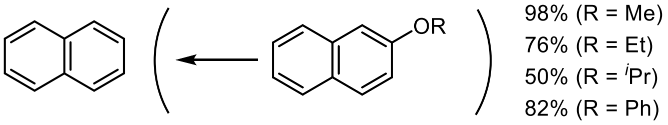
R_f 0.60 (hexane/EtOAc = 20/1). White solid (46 mg, 70%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.34 (s, 12H), 2.54 (s, 3H), 7.14-7.17 (m, 2H), 7.31 (td, *J* = 1.4, 7.8 Hz, 1H), 7.75-7.77 (m, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 22.4, 25.0, 83.5, 124.8, 129.9, 130.9, 136.0, 145.0.

HRMS (EI): Calcd for $C_{13}H_{19}BO_2$ 218.1478, Found 218.1479.

Naphthalene (3w, 3x, 3y, 3z). [CAS: 91-20-3]



The typical procedure was followed using **2w**, **2x**, **2y** or **2z** and the reaction temperature was 100 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product. GC yield of a product from **2w**, **2x**, **2y** or **2z** were 98%, 76%, 50% or 82%, respectively. When using **2z** as a substrate, phenol was also obtained in 75% GC yield.

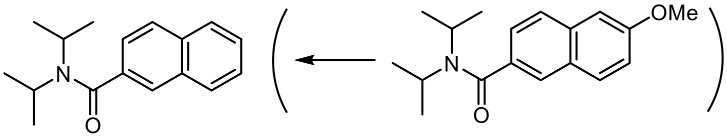
R_f 0.43 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.45-7.48 (m, 4H), 7.82-7.84 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 126.0, 128.0, 133.6.

HRMS (EI): Calcd for $C_{10}H_8$ 128.0626, Found 128.0627.

***N,N*-Diisopropyl-2-naphthamide (3aa).** [CAS: 31609-22-0][7d]



The typical procedure was followed using **2aa**, and the reaction temperature was 100 °C.

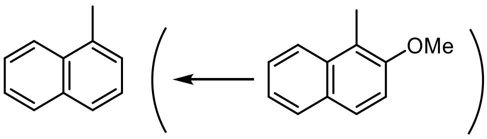
R_f 0.26 (hexane/EtOAc = 40/1). White solid (67 mg, 87%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.37 (br, 12H), 3.73 (br, 2H), 7.42 (dd, *J* = 1.8, 8.3 Hz, 1H), 7.49-7.54 (m, 2H), 7.80 (d, *J* = 0.68 Hz, 1H), 7.83-7.87 (m, 3H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 20.9, 46.1 (br), 51.1 (br), 123.6, 124.9, 126.7, 127.9, 128.3, 128.4, 133.0, 133.2, 136.3, 171.2.

HRMS (EI): Calcd for $C_{17}H_{21}NO$ 255.1623, Found 255.1623.

1-Methylnaphthalene (3ab). [CAS: 90-12-0]



The typical procedure was followed using **2ab**, and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (89%).

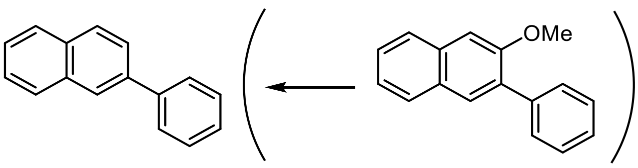
R_f 0.43 (hexane). Colorless oil.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.68 (s, 3H), 7.30 (d, *J* = 7.0 Hz, 1H), 7.36 (t, *J* = 7.0 Hz, 1H), 7.45-7.53 (m, 2H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.72-7.84 (m, 1H), 7.98 (d, *J* = 8.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 19.5, 124.2, 125.6, 125.7, 125.8, 126.5, 126.7, 128.6, 132.7, 133.6, 134.4.

HRMS (EI): Calcd for $C_{11}H_{10}$ 142.0783, Found 142.0785.

2-Phenylnaphthalene (3ac). [CAS: 612-94-2]



The typical procedure was followed using **2ac**, and the reaction temperature was 180 °C.

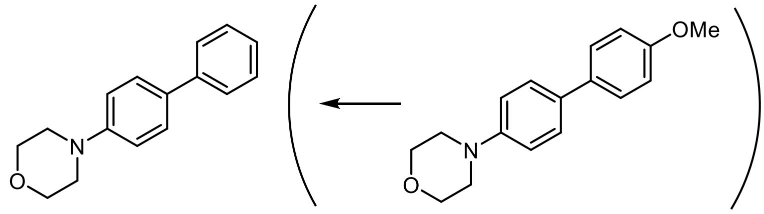
R_f 0.40 (hexane). White solid (56 mg, 91%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.38 (tt, J = 1.4, 7.3 Hz, 1H), 7.46-7.53 (m, 4H), 7.71-7.77 (m, 3H), 7.86-7.93 (m, 3H), 8.05 (d, J = 1.6 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 125.7, 125.9, 126.1, 126.4, 127.5, 127.6, 127.8, 128.3, 128.6, 129.0, 132.7, 133.8, 138.7, 141.3.

HRMS (EI): Calcd for $C_{16}H_{12}$ 204.0939, Found 204.0937.

4-([1,1'-Biphenyl]-4-yl)morpholine (3ae). [CAS: 169963-54-6][37]



The typical procedure was followed using **2ae**, and the reaction temperature was 100 °C.

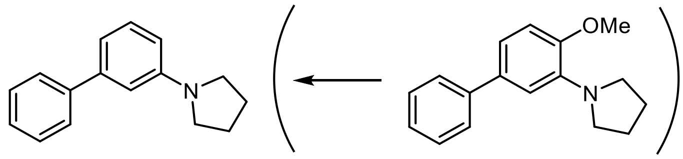
R_f 0.23 (hexane/EtOAc = 4/1). White solid (48 mg, 67%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.21 (t, J = 4.8 Hz, 4H), 3.88 (t, J = 4.8 Hz, 4H), 6.99 (d, J = 8.7 Hz, 2H), 7.29 (t, J = 7.3 Hz, 1H), 7.41 (t, J = 7.3 Hz, 2H), 7.52-7.57 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 49.3, 67.0, 115.9, 126.7, 127.9, 128.8, 132.8, 140.9, 150.6.

HRMS (EI): Calcd for $C_{16}H_{17}NO$ 239.1310, Found 239.1311.

1-([1,1'-Biphenyl]-3-yl)pyrrolidine (3af). [CAS: 852227-07-7]



The typical procedure was followed using **2af**, and the reaction temperature was 180 °C.

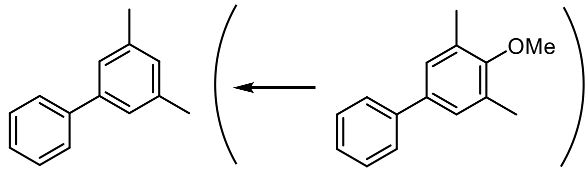
R_f 0.31 (hexane/EtOAc = 40/1). Pale yellow oil (39 mg, 59%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.97 (quin, J = 3.2 Hz, 4H), 3.30 (t, J = 6.4 Hz, 4H), 6.55 (dd, J = 1.8, 8.3 Hz, 1H), 6.74 (t, J = 1.8 Hz, 1H), 6.87 (d, J = 7.6 Hz, 1H), 7.25-7.32 (m, 2H), 7.38-7.42 (m, 2H), 7.58-7.61 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 25.6, 47.8, 110.6, 110.8, 114.7, 127.1, 127.4, 128.6, 129.5, 142.3, 142.4, 148.3.

HRMS (EI): Calcd for $C_{16}H_{17}N$ 223.1361, Found 223.1362.

3,5-Dimethyl-1,1'-biphenyl (3ag). [CAS: 17057-88-4]



The typical procedure was followed using **2ag**, and the reaction temperature was 180 °C.

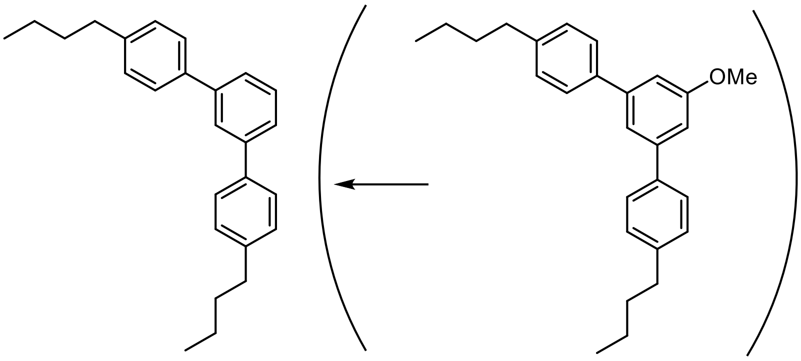
R_f 0.23 (hexane). Colorless oil (31 mg, 56%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.38 (s, 6H), 6.99-7.00 (m, 1H), 7.21 (s, 2H), 7.30-7.34 (m, 1H), 7.40-7.43 (m, 2H), 7.56-7.58 (m, 2H).

^{13}C NMR (CDCl$_3$, 100.53 MHz): δ 21.6, 125.2, 127.2, 127.3, 128.8, 129.0, 138.4, 141.4, 141.6.

HRMS (EI): Calcd for $C_{14}H_{14}$ 182.1096, Found 182.1098.

4,4''-Dibutyl-1,1':3',1''-terphenyl (3ah).



The typical procedure was followed using **2ah**, and the reaction temperature was 100 °C.

R_f 0.31 (hexane). White solid (94 mg, 92%). Mp = 38 °C.

^{1}H NMR (CDCl$_3$, 399.78 MHz): δ 0.95 (t, *J* = 7.4 Hz, 6H), 1.34-1.44 (m, 4H), 1.60-1.68 (m, 4H), 2.65 (t, *J* = 7.4 Hz, 4H), 7.26 (d, *J* = 8.2 Hz, 4H), 7.44-7.48 (m, 1H), 7.52-7.56 (m, 6H), 7.78-7.79 (m, 1H).

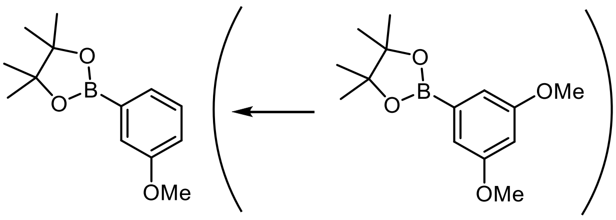
^{13}C NMR (CDCl$_3$, 100.53 MHz): δ 14.1, 22.6, 33.8, 35.5, 125.8, 126.0, 127.2, 129.0, 129.2, 138.7, 141.8, 142.3.

IR (ATR): 3025 w, 2958 m, 2925 m, 2856 m, 2363 w, 1602 w, 1563 w, 1516 m, 1475 m, 1375 w, 1189 w, 1123 w, 1102 w, 1017 w, 895 w, 831 m, 776 s, 729 w, 696 m, 667 w.

MS m/z (% relative intensity): 343 (17), 342 (M^+, 66), 300 (24), 299 (100), 256 (23).

HRMS (EI): Calcd for $C_{26}H_{30}$ 342.2348, Found 342.2347.

2-(3-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3aj). [CAS: 325142-84-5]



The typical procedure was followed using **2aj**, and the reaction temperature was 180 °C.

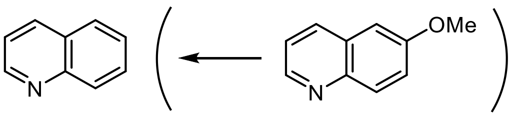
R_f 0.20 (hexane/EtOAc = 20/1). Colorless oil (32 mg, 45%).

^{1}H NMR (CDCl$_3$, 399.78 MHz): δ 1.34 (s, 12H), 3.83 (s, 3H), 7.01 (dd, *J* = 0.92, 8.3 Hz, 1H), 7.28-7.33 (m, 2H), 7.40 (d, *J* = 6.9 Hz, 1H).

^{13}C NMR (CDCl$_3$, 100.53 MHz): δ 25.0, 55.4, 84.0, 118.1, 118.7, 127.3, 129.1, 159.1.

HRMS (EI): Calcd for $C_{13}H_{19}BO_3$ 234.1427, Found 234.1427.

Quinoline (3ak). [CAS: 91-22-5]



The typical procedure was followed using **2ak**, and the reaction temperature was 180 °C.

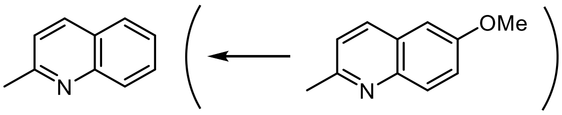
R_f 0.23 (hexane/EtOAc = 3/1). Pale yellow oil (22 mg, 57%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.33-7.39 (m, 1H), 7.49-7.55 (m, 1H), 7.67-7.73 (m, 1H), 7.77-7.81 (m, 1H), 8.10-8.13 (m, 2H), 8.89-8.92 (m, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.1, 126.6, 127.8, 128.3, 129.4, 129.5, 136.1, 148.3, 150.4.

HRMS (EI): Calcd for C_9H_7N 129.0578, Found 129.0577.

2-Methylquinoline (3al). [CAS: 91-63-4]



The typical procedure was followed using **2al**, and the reaction temperature was 180 °C.

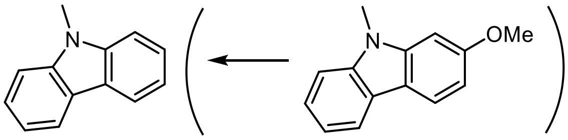
R_f 0.20 (hexane/EtOAc = 4/1). Pale yellow oil (24 mg, 55%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.75 (s, 3H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.46-7.50 (m, 1H), 7.66-7.70 (m, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 8.03 (t, *J* = 8.4 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 25.5, 122.1, 125.8, 126.6, 127.6, 128.7, 129.6, 136.3, 148.0, 159.1.

HRMS (EI): Calcd for $C_{10}H_9N$ 143.0735, Found 143.0735.

9-Methyl-9*H*-carbazole (3am). [CAS: 1484-12-4]



The typical procedure was followed using **2am**, and the reaction temperature was 180 °C.

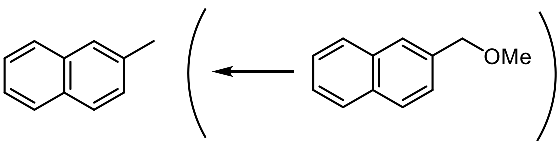
R_f 0.21 (hexane/EtOAc = 40/1). White solid (49 mg, 91%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.83 (s, 3H), 7.23 (t, *J* = 7.8 Hz, 2H), 7.39 (d, *J* = 7.8 Hz, 2H), 7.45-7.49 (m, 2H), 8.09 (d, *J* = 7.8 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 29.2, 108.5, 119.0, 120.4, 122.9, 125.8, 141.1.

HRMS (EI): Calcd for $C_{13}H_{11}N$ 181.0891, Found 181.0889.

2-Methylnaphthalene (3an). [CAS: 91-57-6]



The typical procedure was followed using **2an**, and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (82%).

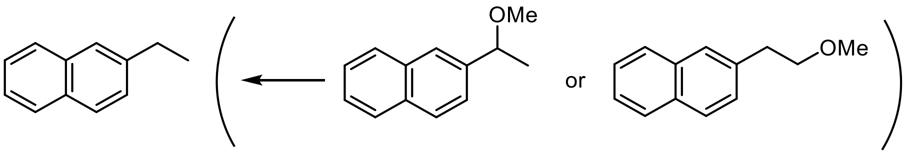
R_f 0.46 (hexane). Colorless oil.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.51 (s, 3H), 7.30 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.37-7.45 (m, 2H), 7.60 (s, 1H), 7.72-7.75 (m, 2H), 7.78 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 21.9, 125.1, 126.0, 127.0, 127.4, 127.7, 127.8, 128.2, 131.8, 133.8, 135.6.

HRMS (EI): Calcd for $C_{11}H_{10}$ 142.0783, Found 142.0782.

2-Ethylnaphthalene (3ao, 3as). [CAS: 939-27-5]



The typical procedure was followed using **2ao**, and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (97%). The typical procedure was followed using **2as** except that $Ni(cod)_2$ (20 mol%) and $IMes^{Me}$ (40 mol%) were used , and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (93%).

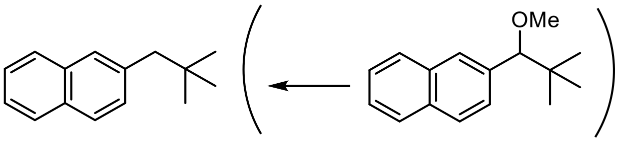
R_f 0.47 (hexane). Colorless oil.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.32 (t, *J* = 7.6 Hz, 3H), 2.81 (q, *J* = 7.6 Hz, 2H), 7.35 (dd, *J* = 1.8, 8.7 Hz, 1H), 7.39-7.46 (m, 2H), 7.62 (s, 1H), 7.76-7.81 (m, 3H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.7, 29.2, 125.1, 125.6, 126.0, 127.2, 127.5, 127.7, 127.9, 132.0, 133.8, 141.9.

HRMS (EI): Calcd for $C_{12}H_{12}$ 156.0939, Found 156.0936.

2-Neopentylnaphthalene (3ap). [CAS: 61760-11-0][38]



The typical procedure was followed using **2ap**, and the reaction temperature was 180 °C.

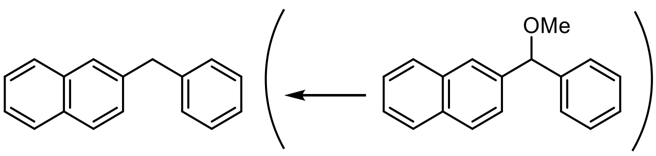
R_f 0.37 (hexane). White solid (27 mg, 46%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.95 (s, 9H), 2.66 (s, 2H), 7.29 (dd, *J* = 1.8, 8.2 Hz, 1H), 7.40-7.47 (m, 2H), 7.57 (s, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.78-7.82 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 29.6, 32.3, 50.5, 125.2, 125.8, 127.0, 127.7, 128.7, 129.6, 132.0, 133.4, 137.6.

HRMS (EI): Calcd for $C_{15}H_{18}$ 198.1409, Found 198.1407.

2-Benzylnaphthalene (3aq). [CAS: 613-59-2]



The typical procedure was followed using **2aq**, and the reaction temperature was 180 °C.

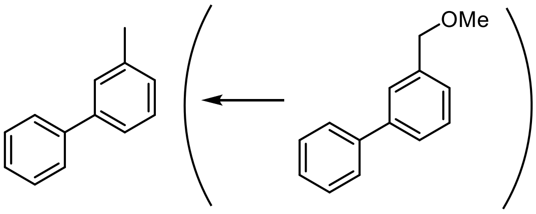
R_f 0.20 (hexane/EtOAc = 40/1). Colorless oil (56 mg, 86%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 4.13 (s, 2H), 7.18-7.23 (m, 3H), 7.27-7.32 (m, 3H), 7.39-7.46 (m, 2H), 7.62 (s, 1H), 7.73-7.79 (m, 3H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 42.2, 125.5, 126.1, 126.3, 127.2, 127.6, 127.7, 127.8, 128.2, 128.6, 129.2, 132.2, 133.7, 138.7, 141.1.

HRMS (EI): Calcd for $C_{17}H_{14}$ 218.1096, Found 218.1095.

3-Methyl-1,1'-biphenyl (3ar). [CAS: 643-93-6][39]



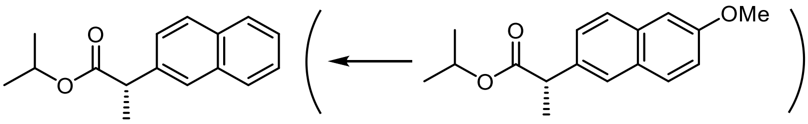
The typical procedure was followed using **2ar**, and the reaction temperature was 180 °C. The yield was determined by GC analysis using eicosane as an internal standard due to volatility of the product (59%).

R_f 0.23 (hexane). Colorless oil.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.42 (s, 3H), 7.16 (d, *J* = 7.3 Hz, 1H), 7.33 (t, *J* = 7.3 Hz, 2H), 7.38-7.45 (m, 4H), 7.58 (d, *J* = 7.3 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 21.7, 124.4, 127.3, 128.1, 128.8, 128.9, 138.5, 141.3, 141.5. HRMS (EI): Calcd for $C_{13}H_{12}$ 168.0939, Found 168.0938.

Isopropyl (*S*)-2-(6-methoxynaphthalen-2-yl)propanoate (3at).



The typical procedure was followed using **2at** except that NaOAc was not added, and the reaction temperature was 100 °C.

R_f 0.20 (hexane/EtOAc = 20/1). Colorless oil (48 mg, 66%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.12 (d, *J* = 6.4 Hz, 3H), 1.22 (d, *J* = 6.4 Hz, 3H), 1.57 (d, *J* = 7.3 Hz, 3H), 3.84 (q, *J* = 7.3 Hz, 1H), 5.01 (quintet, *J* = 6.4 Hz, 1H), 7.42-7.50 (m, 3H), 7.74 (s, 1H), 7.79-7.82 (m, 3H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 19.2, 22.1, 22.3, 46.4, 68.6, 126.2, 126.3, 126.6, 126.7, 128.2, 128.4, 128.7, 133.1, 134.0, 138.8, 174.6.

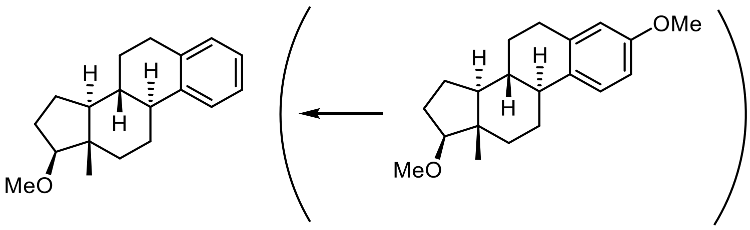
IR (ATR): 2979 w, 2935 w, 1716 s, 1600 w, 1508 w, 1453 w, 1374 m, 1319 w, 1249 w, 1184 s, 1104 s, 1017 w, 950 w, 928 w, 892 w, 858 w, 820 m, 795 w, 746 m.

MS m/z (% relative intensity): 242 (M^+, 34), 155 (100), 153 (23).

HRMS (EI): Calcd for $C_{16}H_{18}O_2$ 242.1307, Found 242.1304.

$[\alpha]_D^{20}$ = +9.2 (c = 9.8 × 10^{-2}, $CHCl_3$).

(8*R*,9*S*,13*S*,17*S*)-17-Methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene (3au).

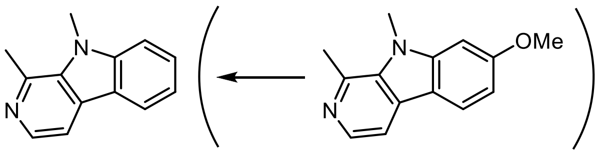


The typical procedure was followed using **2au**, and the reaction temperature was 180 °C.

R_f 0.23 (hexane/EtOAc = 20/1). White solid (61 mg, 75%). Mp = 131 °C.

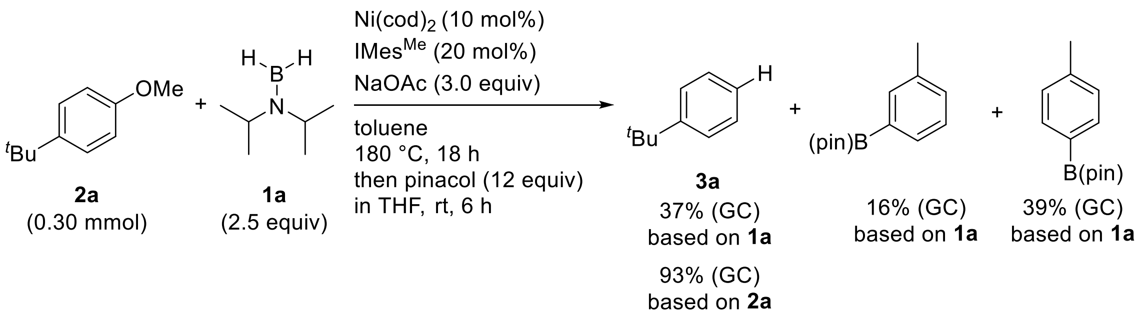
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.79 (s, 3H), 1.07-1.25 (m, 3H), 1.31-1.59 (m, 3H), 1.66-1.73 (m, 1H), 1.88 (d, *J* = 12 Hz, 1H), 2.02-2.12 (m, 2H), 2.23-2.33 (m, 3H), 2.85-2.88 (m, 2H), 3.32 (t, *J* = 8.2 Hz, 1H), 3.38 (s, 3H), 7.07-7.16 (m, 3H), 7.30 (d, *J* = 6.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 11.7, 23.2, 26.3, 27.3, 27.9, 29.7, 38.2, 38.5, 43.3, 44.6, 50.6, 58.0, 90.9, 125.5, 125.6, 125.7, 129.1, 136.8, 140.5.
IR (ATR): 2935 m, 2866 m, 1486 w, 1446 w, 1363 w, 1266 w, 1190 m, 1168 w, 1134 w, 1100 s, 1011 w, 990 w, 820 w, 769 w, 747 s.
MS m/z (% relative intensity): 270 (M^+, 41), 238 (22), 198 (17), 197 (100), 196 (11), 144 (25), 143 (17), 142 (17), 141 (14), 129 (21), 128 (14), 117 (25), 115 (11).
HRMS (EI): Calcd for $C_{19}H_{26}O$ 270.1984, Found 270.1986.
$[\alpha]_D^{20}$ = +28.0 (c = 7.7 × 10^{-2}, $CHCl_3$).

1,9-Dimethyl-9*H*-pyrido[3,4-*b*]indole (3av). [CAS: 16498-64-9]



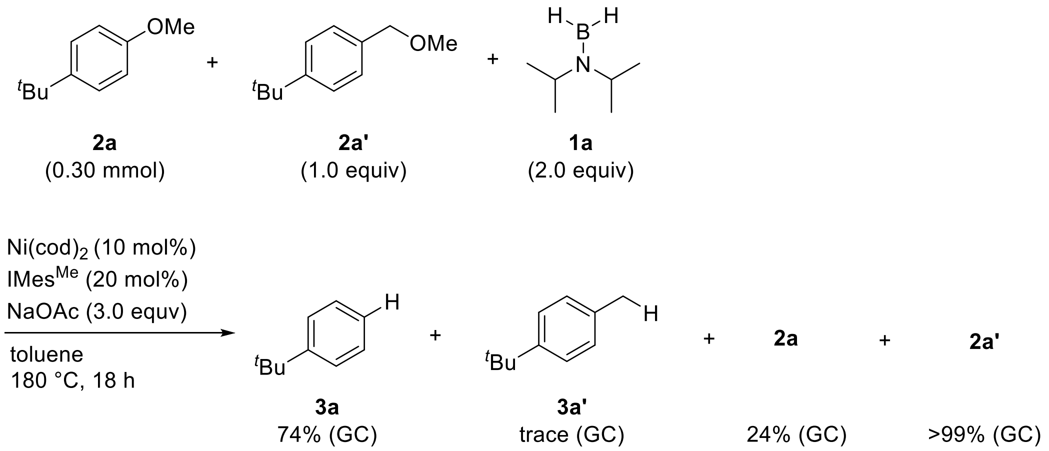
The typical procedure was followed using **2av**, and the reaction temperature was 180 °C.
R_f 0.43 (NH silica, hexane/EtOAc = 1/1). White solid (41 mg, 70%).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.08 (s, 3H), 4.12 (s, 3H), 7.25-7.27 (m, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.56-7.61 (m, 1H), 7.81 (d, *J* = 5.3 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 8.30 (d, *J* = 5.3 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 23.8, 32.4, 109.5, 113.0, 119.7, 121.2, 121.6, 128.2, 128.9, 136.0, 138.1, 141.8, 142.2.
HRMS (EI): Calcd for $C_{13}H_{12}N_2$ 196.1000, Found 196.1003.

3.4.5 The Observation of C(aryl)-H Borylation of Solvent Toluene by the Addition of Pinacol



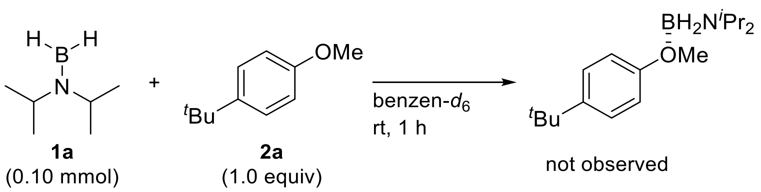
In a glovebox filled with nitrogen, $Ni(cod)_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), IMes^{Me} (20 mg, 0.060 mmol, 0.20 equiv), NaOAc (74 mg, 0.90 mmol, 3.0 equiv) and toluene (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. **2a** (0.30 mmol, 1.0 equiv), and **1a** (68 mg, 0.60 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 180 °C for 18 h. After the reaction mixture was cooled to room temperature, pinacol (424 mg, 3.6 mmol, 12 equiv) in dehydrated THF (2.0 mL) was added to the mixture, and then stirred at room temperature for 6 h under N_2. The resulting mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. The borylated products of the toluene solvent were observed in 55% total yields based on **1a**, along with the generation of the deoxygenated product **3a** in 37% yield based on **1a**. This result indicates that significant amount of **1a** is consumed by C-H borylation of solvent toluene.

3.4.6 Competitive Reduction of 2a and 1-(*tert*-Butyl)-4-(methoxymethyl)benzene (2a') with 1a under the Standard Reaction Conditions

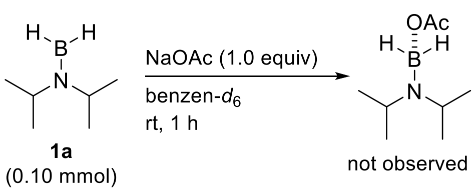


In a glovebox filled with nitrogen, Ni(cod)$_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), IMes^{Me} (20 mg, 0.060 mmol, 0.20 equiv) and toluene (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv), **2a** (49 mg, 0.30 mmol, 1.0 equiv), **2a'** (53 mg, 0.30 mmol, 1.0 equiv) and **1a** (68 mg, 0.60 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 180 °C for 18 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. **3a** was obtained from **2a** in 74% GC yield. In contrast, this reaction didn't afford **3a'** from **2a'**.

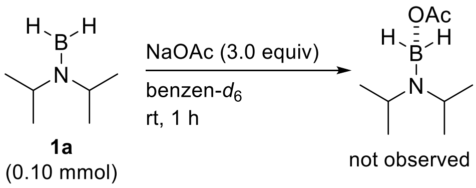
3.4.7 The Attempted Observation of the Interaction between Reagents by ^{11}B NMR Spectroscopy



In a glovebox filled with nitrogen, **1a** (11 mg, 1.0 equiv), **2a** (16 mg, 0.10 mmol, 1.0 equiv) and benzene-d_6 (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 1 h at room temperature. ^{11}B NMR analysis of the resulting mixture showed no indication of the formation of a **1a**/**2a** complex.



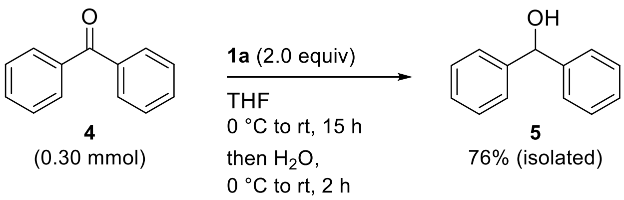
In a glovebox filled with nitrogen, **1a** (11 mg, 1.0 equiv), NaOAc (7.4 mg, 0.10 mmol, 1.0 equiv) and benzene-d_6 (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 1 h at room temperature. ^{11}B NMR analysis of the resulting mixture did not indicate the formation of the complex of **1a** with NaOAc.



In a glovebox filled with nitrogen, **1a** (11 mg, 1.0 equiv), NaOAc (7.4 mg, 0.10 mmol, 1.0 equiv) and benzene-d_6 (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 1 h at room temperature. ^{11}B NMR analysis of the resulting mixture did not indicate the formation of the complex of **1a** with NaOAc.

In summary, we were unable to obtain any direct evidence of interaction between **1a** and **2a** or NaOAc by ^{11}B NMR, probably because the equilibrium favors the uncomplexed forms.

3.4.8 Reduction of 4 by Using 1a in the Absence of a Catalyst (5). [CAS: 91-01-0]



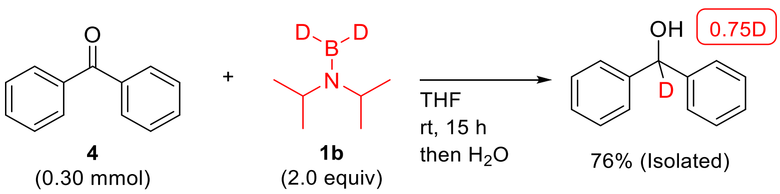
1a (68 mg, 0.60 mmol, 2.0 equiv) was added dropwise to a solution of **4** (55 mg, 0.30 mmol, 1.0 equiv) in dehydtrated THF (5.0 mL), and the reaction mixture was stirred at 0 °C for 15 min. The mixture was then allowed to warm to room temperature and stirred for 15 h. H_2O (5.0 mL) was added slowly to the reaction mixture at 0 °C and it was stirred at room temperature for 2 h. After the solvent was evaporated in vacuo, H_2O (10 mL) was added, and the residue was then extracted with CH_2Cl_2 (10 mL × 3). The combined organic extracts were dried over Na_2SO_4. The solvent was then removed under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc (10/1). The filtrate was concentrated in vacuo to give **5** as a white solid (42 mg, 76%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.31 (br, 1H), 5.81 (s, 1H), 7.23-7.27 (m, 2H), 7.30-7.37 (m, 8H).

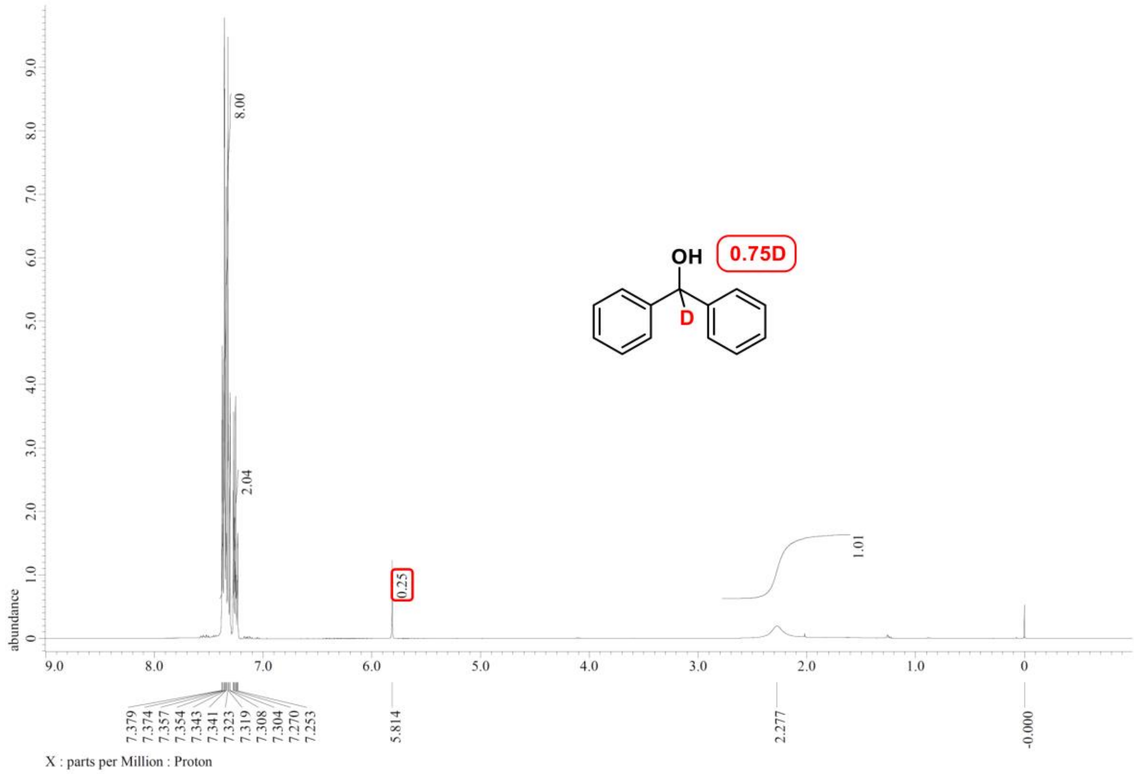
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 76.4, 126.7, 127.7, 128.6, 143.9.

HRMS (EI): Calcd for $C_{13}H_{12}O$ 184.0888, Found 184.0888.

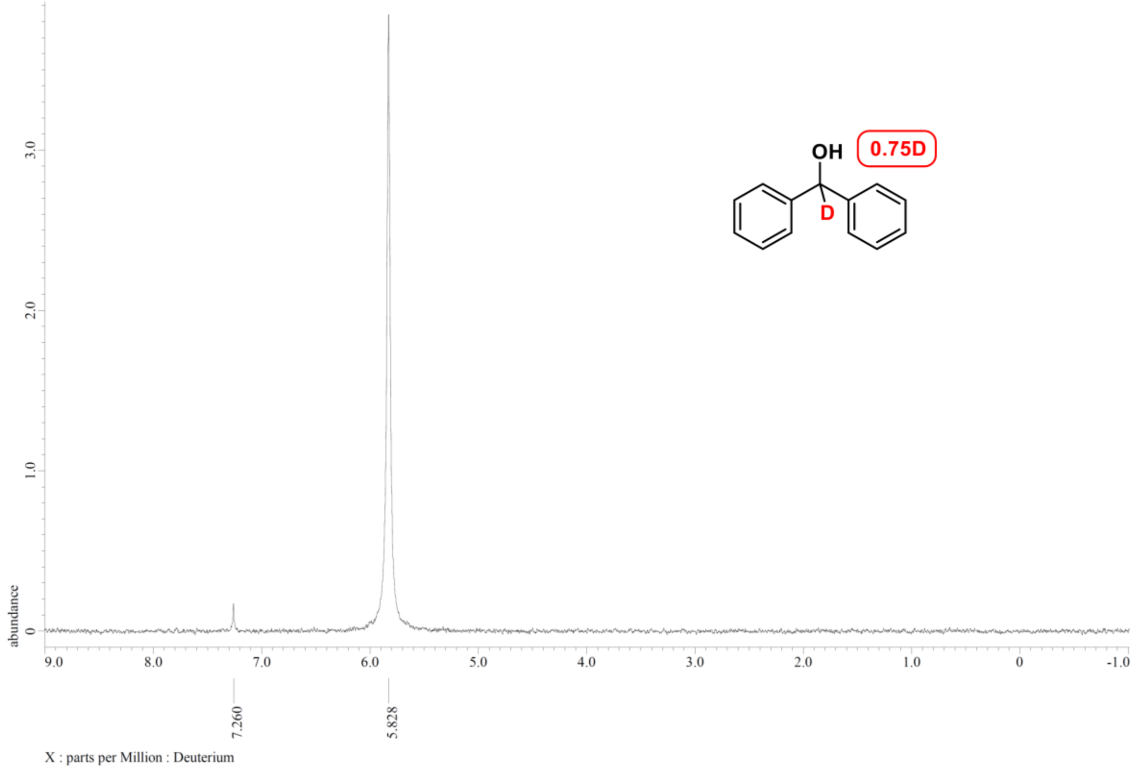
3.4.9 Deuterium Labeling Studies



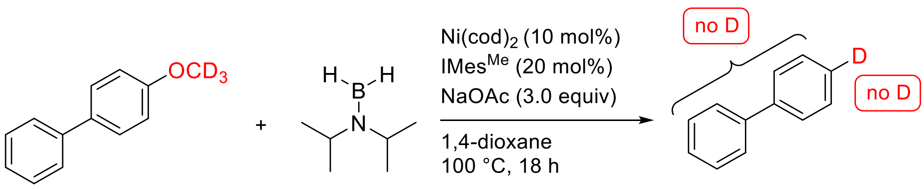
1b (69 mg, 0.60 mmol, 2.0 equiv) was added dropwise to a solution of **4** (55 mg, 0.30 mmol, 1.0 equiv) in dehydtrated THF (5.0 mL), and the reaction mixture was stirred at 0 °C for 15 min. The mixture was then allowed to warm to room temperature and stirred for 15 h. H_2O (5.0 mL) was added slowly to the reaction mixture at 0 °C and it was stirred at room temperature for 2 h. After the solvent was evaporated in vacuo, H_2O (10 mL) was added, and the residue was then extracted with CH_2Cl_2 (10 mL × 3). The combined organic extracts were dried over Na_2SO_4. The solvent was then removed under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc (10/1). The filtrate was concentrated in vacuo to give a corresponding alcohol as a white solid (42 mg, 76%). ^{1}H NMR analysis of the product revealed the level of deuterium incorporation to be 75% based on the integration value of the resonance signal appeared at 5.8 ppm.



^{1}H NMR of generated alcohol with deuterium incorporation in $CDCl_3$

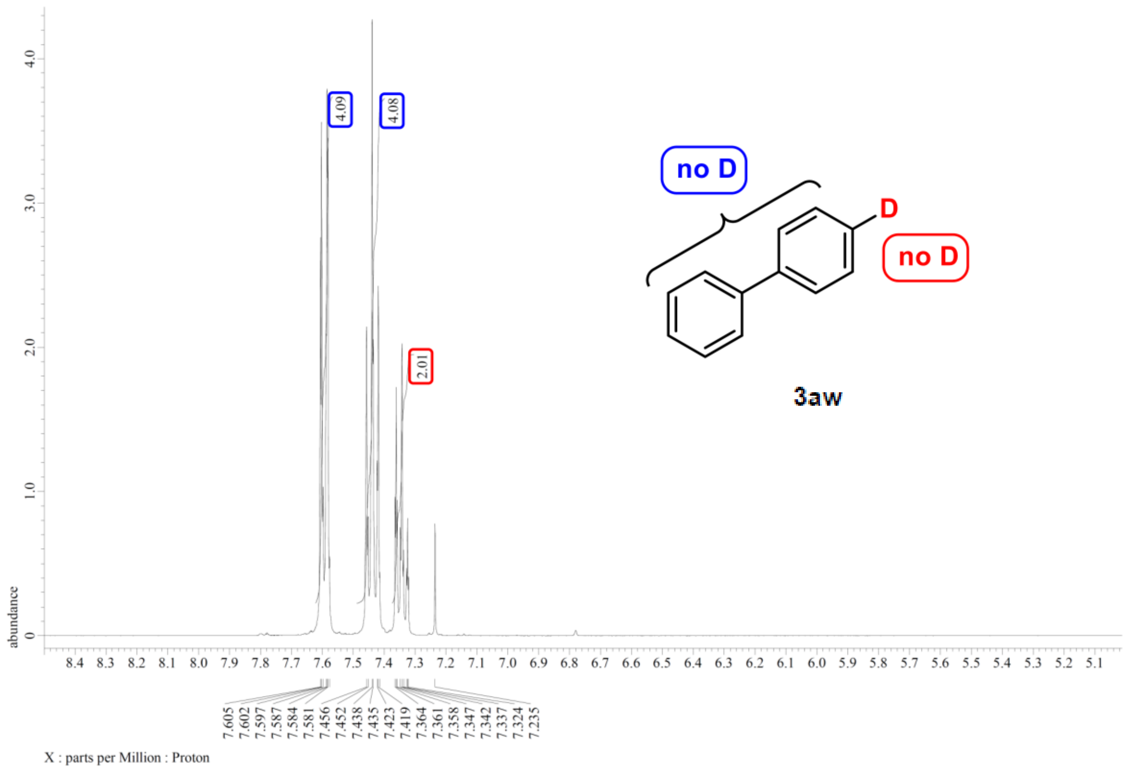


^2H NMR of generated alcohol with deuterium incorporation in $CDCl_3$

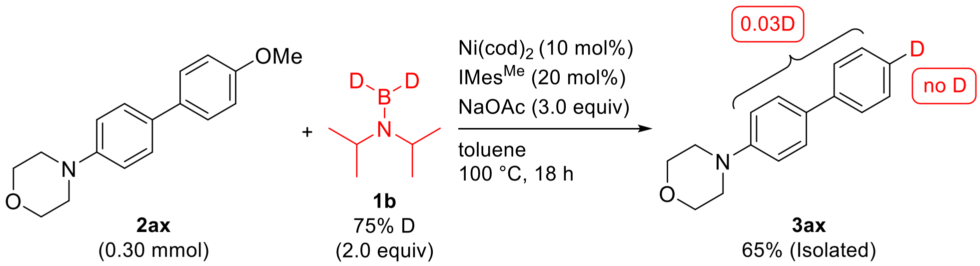


2aw (0.30 mmol) + **1a** (2.0 equiv) → **3aw** 37% (isolated)

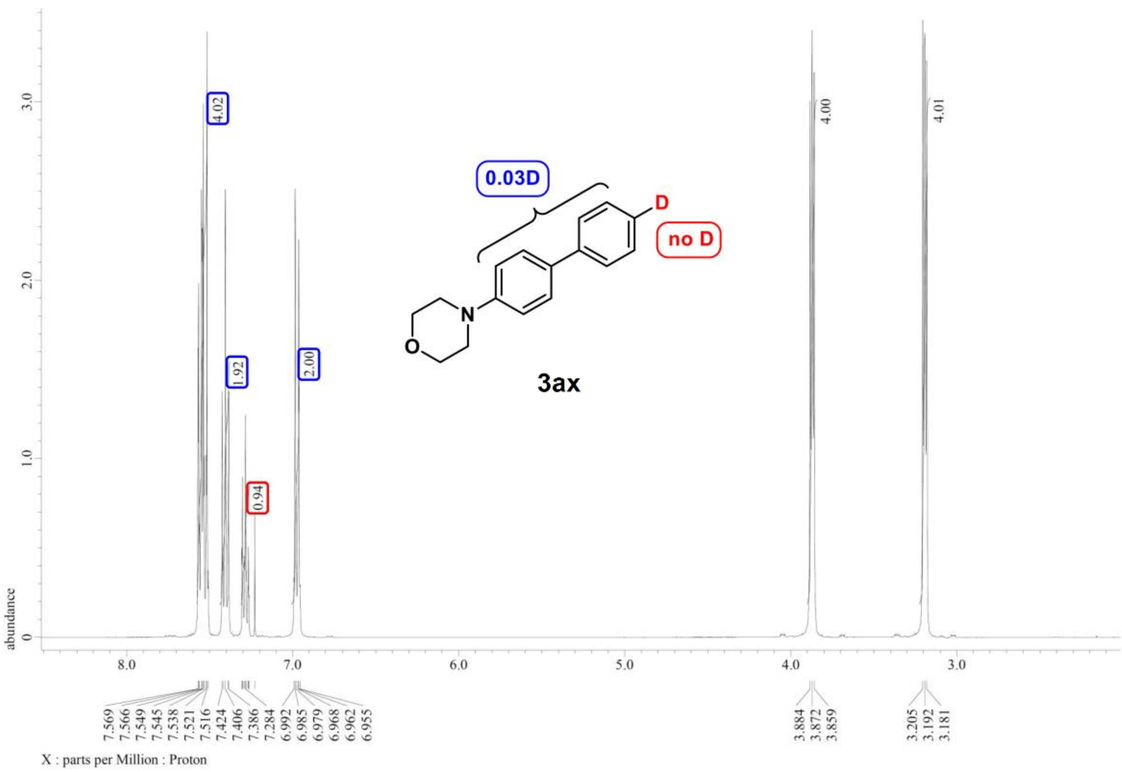
In a glovebox filled with nitrogen, $Ni(cod)_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), $IMes^{Me}$ (20 mg, 0.060 mmol, 0.20 equiv) and 1,4-dioxane (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv), **2aw** (56 mg, 0.30 mmol, 1.0 equiv), and **1a** (68 mg, 0.60 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 100 °C for 18 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. The crude mixture was concentrated under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane. The filtrate was concentrated in vacuo to give a pure reduced product **3aw** (17 mg, 37%) without the deuterium incorporation. This result suggested that, unlike our previously reported method,[7d] β-hydrogen elimination from the oxidative addition complex (Ar-Ni-OMe) is not involved as a major pathway in this catalytic system.



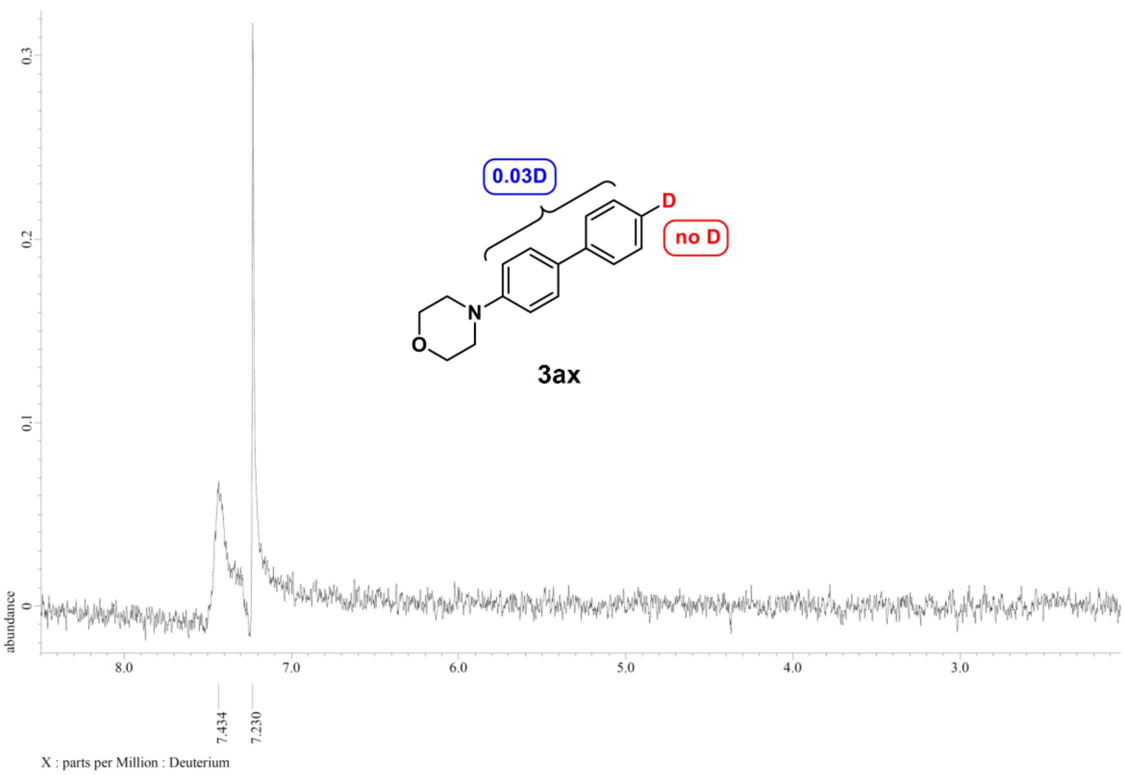
^{1}H NMR of **3aw** in $CDCl_3$



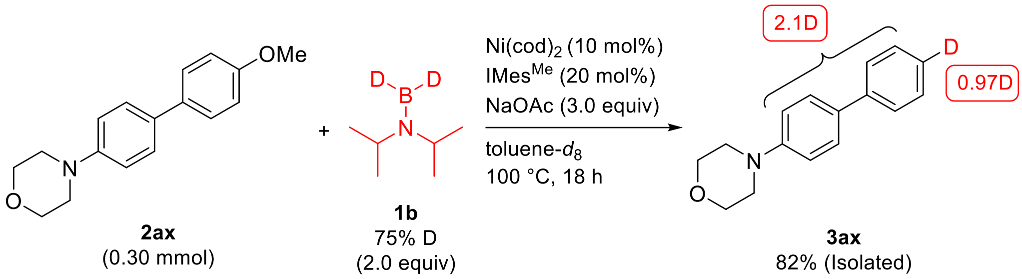
In a glovebox filled with nitrogen, $Ni(cod)_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), $IMes^{Me}$ (20 mg, 0.060 mmol, 0.20 equiv) and toluene (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv), **2ax** (81 mg, 0.30 mmol, 1.0 equiv), and **1b** (69 mg, 0.60 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 100 °C for 18 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. The crude mixture was concentrated under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc (5/1). The filtrate was concentrated in vacuo to give a pure reduced product **3ax** (47 mg, 65%). The deuterium was not incorporated in the product **3ax**.



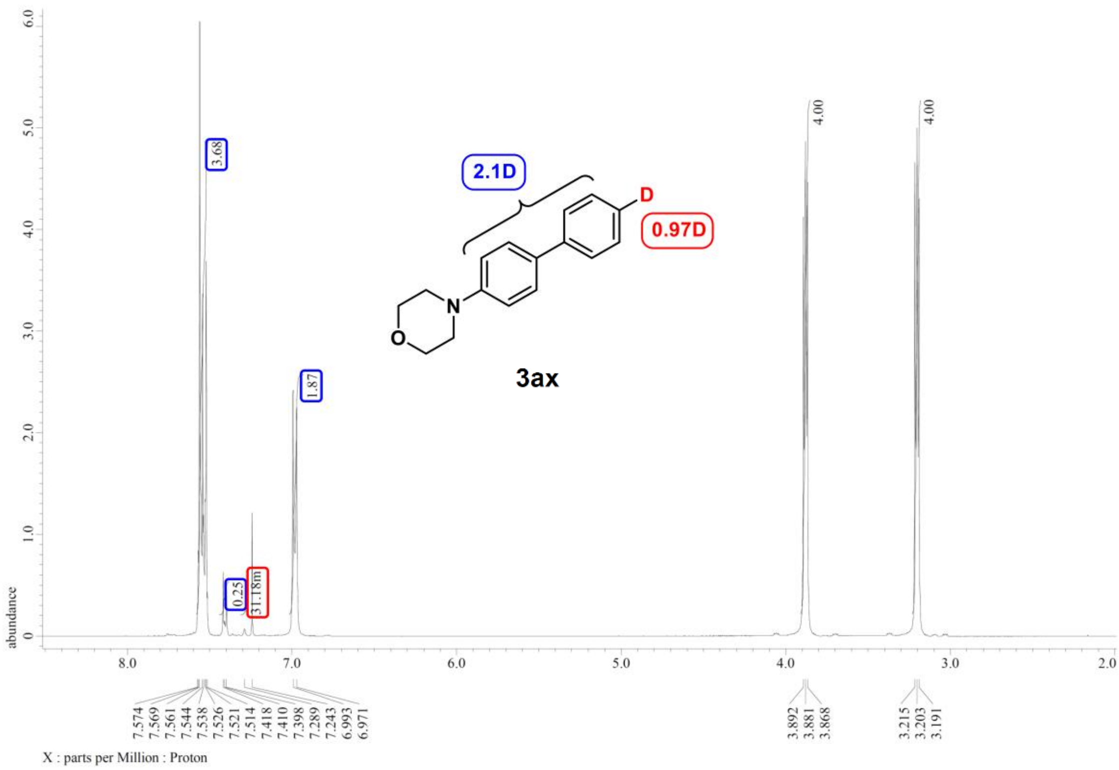
^{1}H NMR of **3ax** with deuterium incorporation in $CDCl_3$



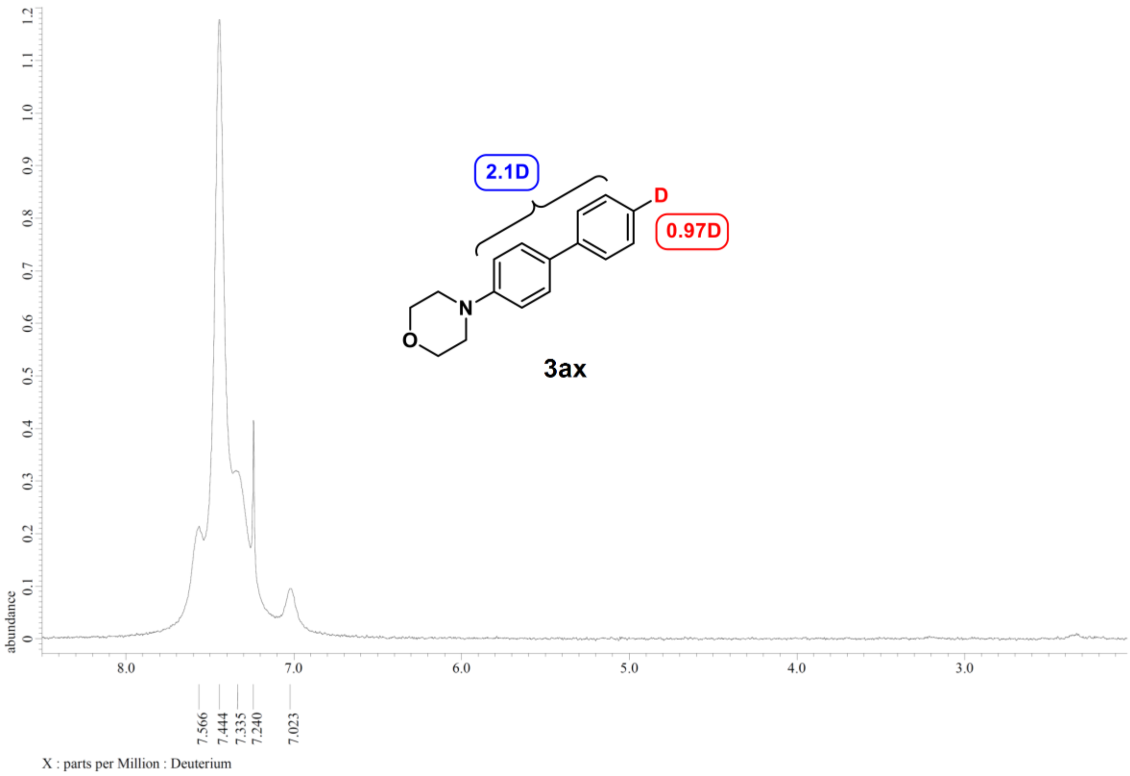
^{2}H NMR of **3ax** with deuterium incorporation in $CDCl_3$



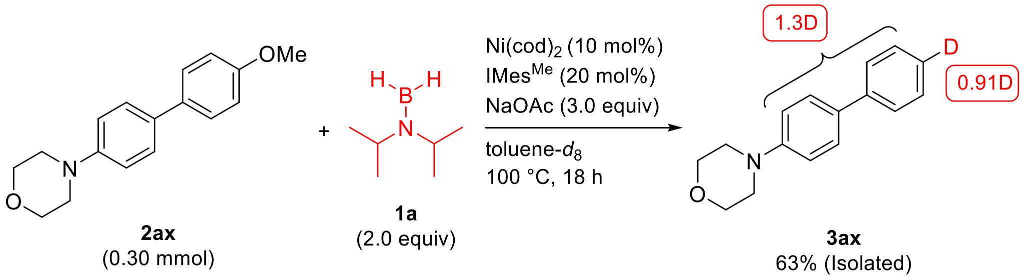
In a glovebox filled with nitrogen, Ni(cod)$_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), IMes^{Me} (20 mg, 0.060 mmol, 0.20 equiv) and toluene-d_8 (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv), **2ax** (81 mg, 0.30 mmol, 1.0 equiv), and **1b** (69 mg, 0.60 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 100 °C for 18 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. The crude mixture was concentrated under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc (5/1). The filtrate was concentrated in vacuo to give a pure reduced product **3ax** (60 mg, 82%). In contrast, 97% deuterium was incorporated at the ipso position of the product, when toluene-d_8 was used as the reaction solvent instead of toluene, which indicated that an H/D exchange reaction was occurring between the reduced product and toluene solvent. Due to this H/D exchange reaction, deuterium was also incorporated at other aromatic C-H bonds of the product **3ax**.



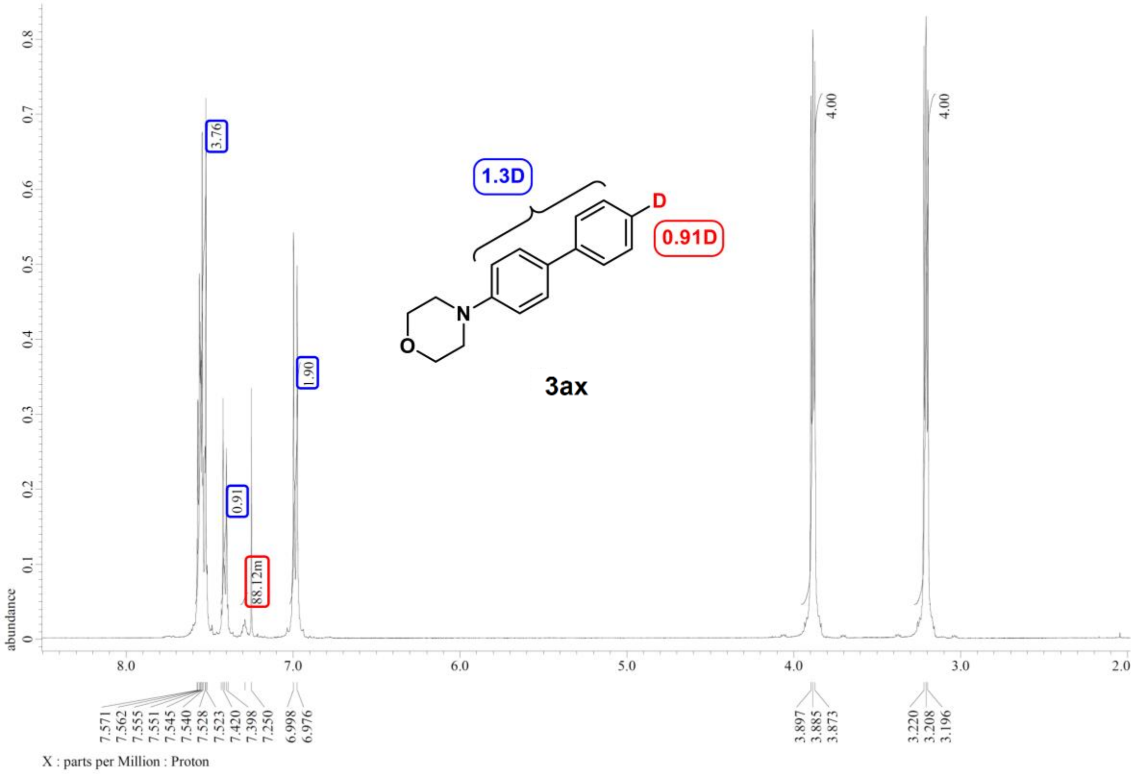
^{1}H NMR of **3ax** with deuterium incorporation in $CDCl_3$



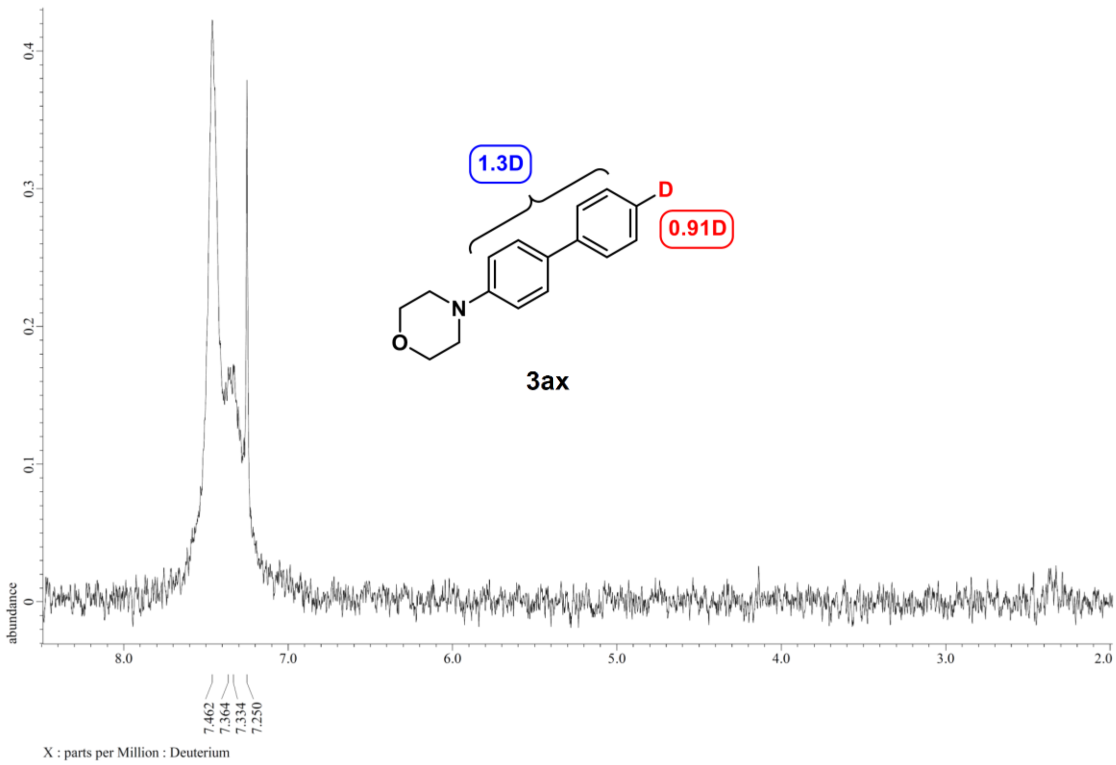
^{2}H NMR of **3ax** with deuterium incorporation in $CDCl_3$



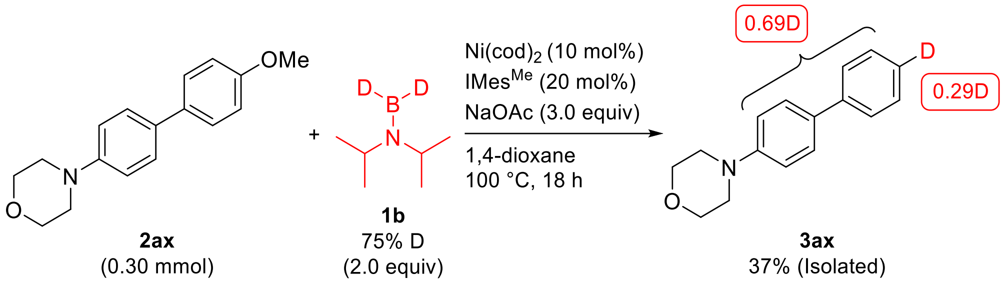
In a glovebox filled with nitrogen, Ni(cod)$_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), IMes^{Me} (20 mg, 0.060 mmol, 0.20 equiv) and toluene-d_8 (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv), **2ax** (81 mg, 0.30 mmol, 1.0 equiv), and **1a** (68 mg, 0.60 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 100 °C for 18 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. The crude mixture was concentrated under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc (5/1). The filtrate was concentrated in vacuo to give a pure reduced product **3ax** (45 mg, 63%). 91% deuterium was incorporated at the ipso position of the product in the reaction of **2ax** with **1a** in toluene. This result clarified that the source of deuterium is derived from toluene solvent.



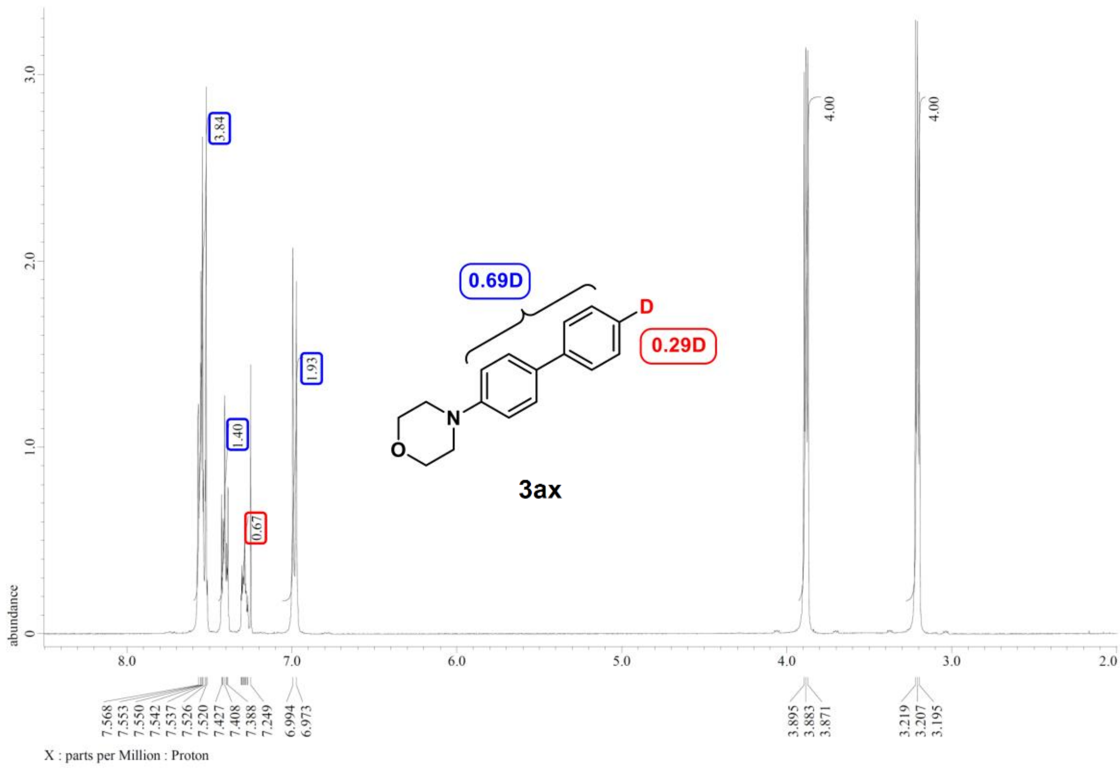
[1]H NMR of **3ax** with deuterium incorporation in $CDCl_3$



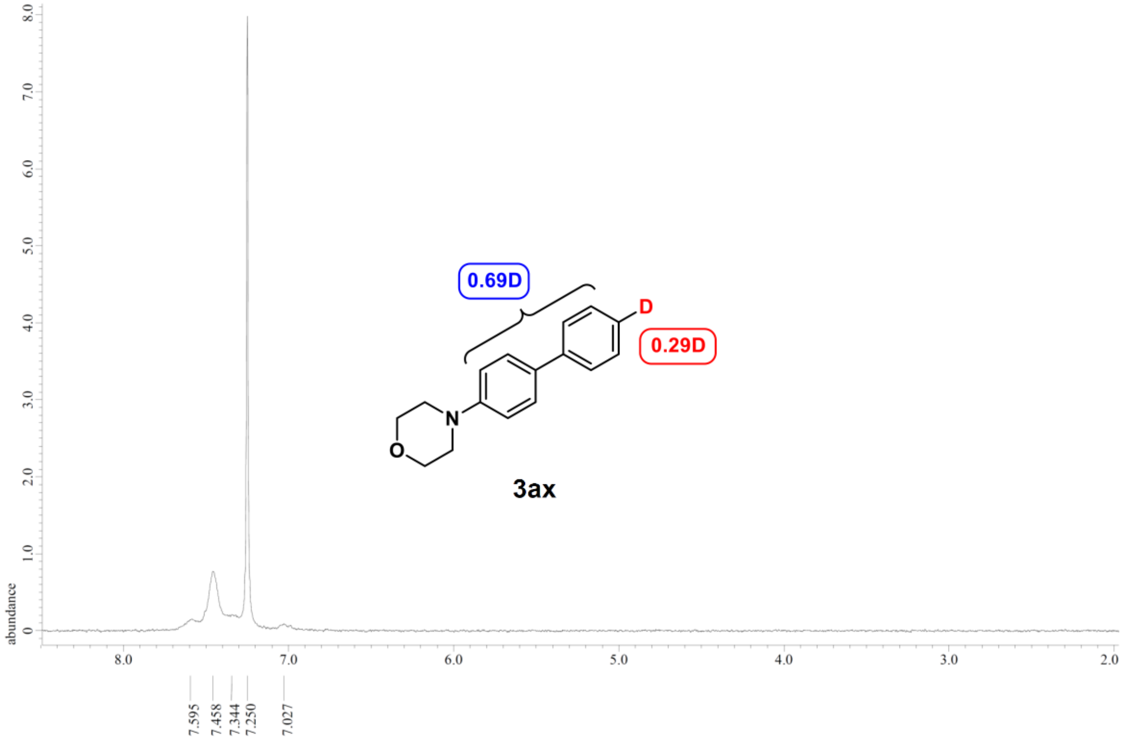
[2]H NMR of **3ax** with deuterium incorporation in $CDCl_3$



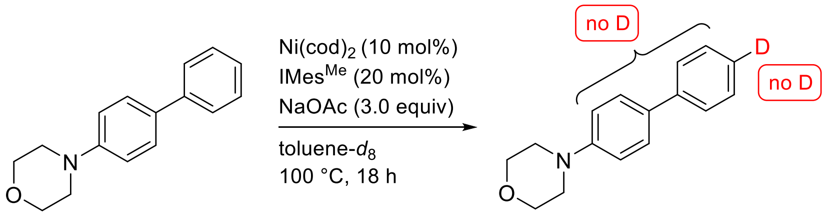
In a glovebox filled with nitrogen, Ni(cod)$_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), IMes^{Me} (20 mg, 0.060 mmol, 0.20 equiv) and 1,4-dioxane (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv), **2ax** (81 mg, 0.30 mmol, 1.0 equiv), and **1b** (69 mg, 0.60 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 100 °C for 18 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. The crude mixture was concentrated under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc (5/1). The filtrate was concentrated in vacuo to give a pure reduced product **3ax** (27 mg, 37%). To avoid the H/D exchange reaction with the solvent, we also conducted the reaction of **2ax** with **1b** in 1,4-dioxane. However, an H/D scrambling between aromatic C-H bonds in **2ax** and **3ax** still hampered probing of the origin of the incorporated hydride.



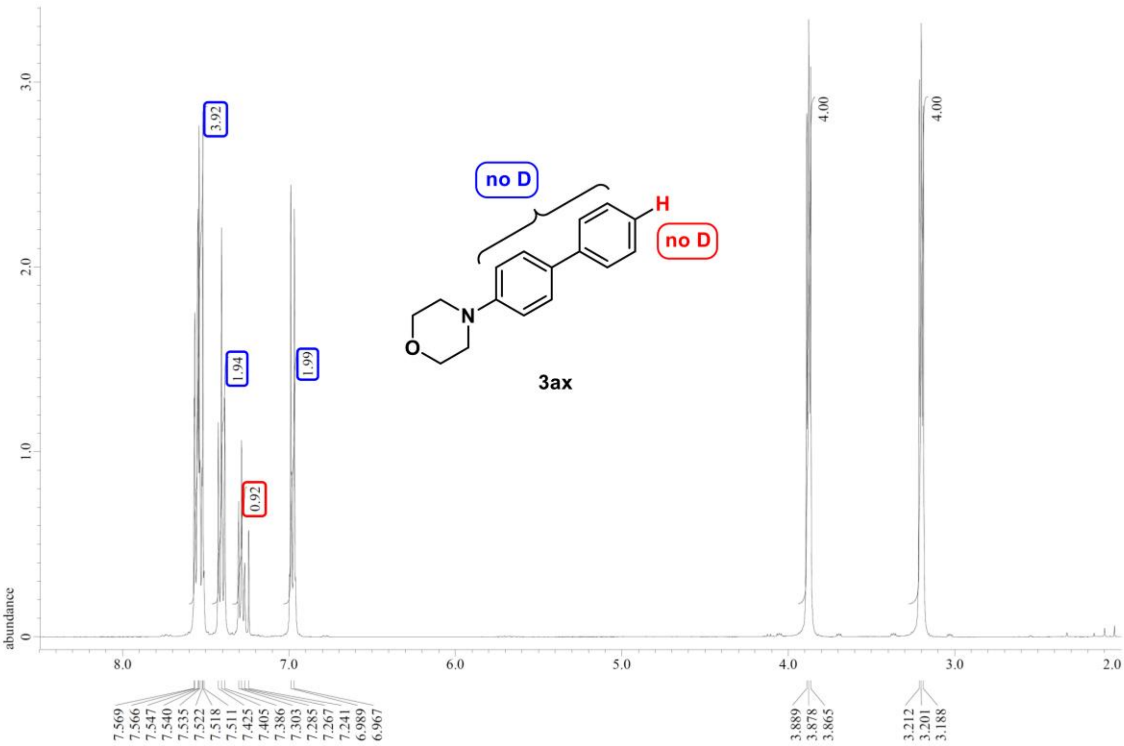
^{1}H NMR of **3ax** with deuterium incorporation in $CDCl_3$



^{2}H NMR of **3ax** with deuterium incorporation in $CDCl_3$



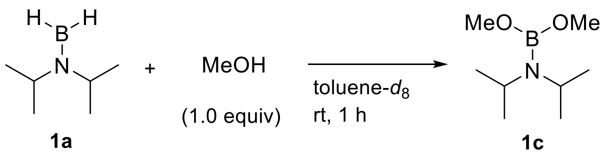
In a glovebox filled with nitrogen, $Ni(cod)_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), IMes^{Me} (20 mg, 0.060 mmol, 0.20 equiv) and toluene-d_8 (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv) and **3ax** (81 mg, 0.30 mmol, 1.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 100 °C for 18 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. The crude mixture was concentrated under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc (5/1). The filtrate was concentrated in vacuo to give a pure reduced product **3ax** (68 mg, 95%). This result indicates that an H/D exchange reaction didn't occur directly between the reduced product and toluene solvent.



^{1}H NMR of **3ax** with deuterium incorporation in $CDCl_3$

Although the rapid H/D exchange between **1a** and aromatic C-H bonds has complicated these results of the labeling study, the source of hydride for the deoxygenation of C(aryl)-O bonds is most likely to be derived from **1a**.

3.4.10 Synthesis of Dimethoxyaminoborane (1c)

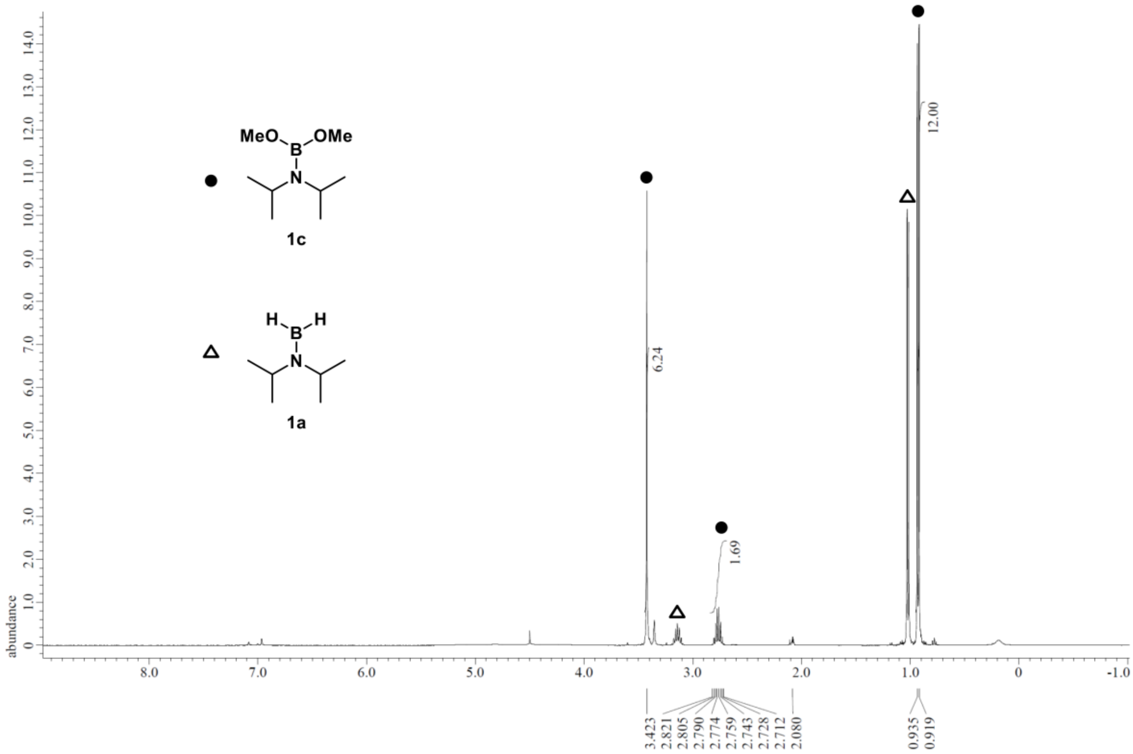


In a glovebox filled with nitrogen, dehydtrated MeOH (9.6 mg, 0.30 mmol, 1.0 equiv) was added to a solution of **1a** (33 mg, 0.30 mmol, 1.0 equiv) in toluene-d_8 (0.50 mL), and stirred for 1 h at room temperature. After the reaction, the generation of **1c** was observed by ^{1}H NMR and ^{11}B NMR. However, unreacted **1a** was remained in this reaction mixture.

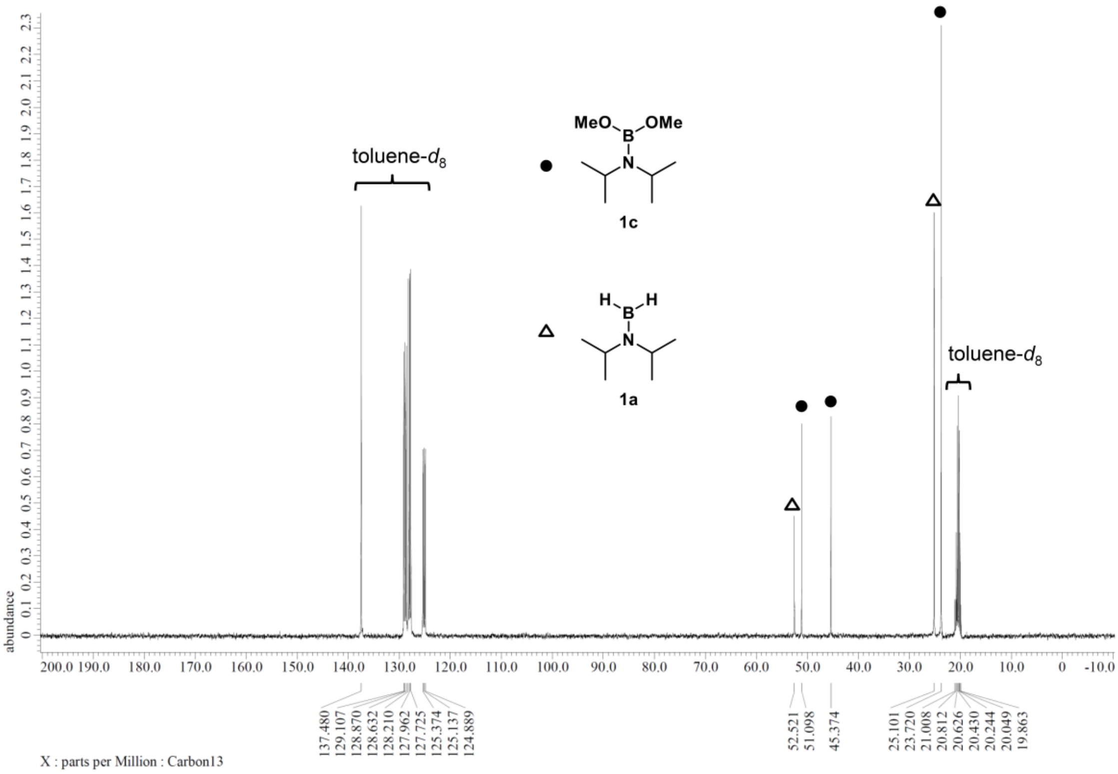
^{1}H NMR (toluene-d_8, 399.78 MHz): δ 0.93 (d, J = 6.2 Hz, 12 H), 2.78 (octet, J = 6.2 Hz, 2H), 3.42 (s, 6H).

^{13}C NMR (toluene-d_8, 100.53 MHz): δ 23.7, 45.4, 51.1.

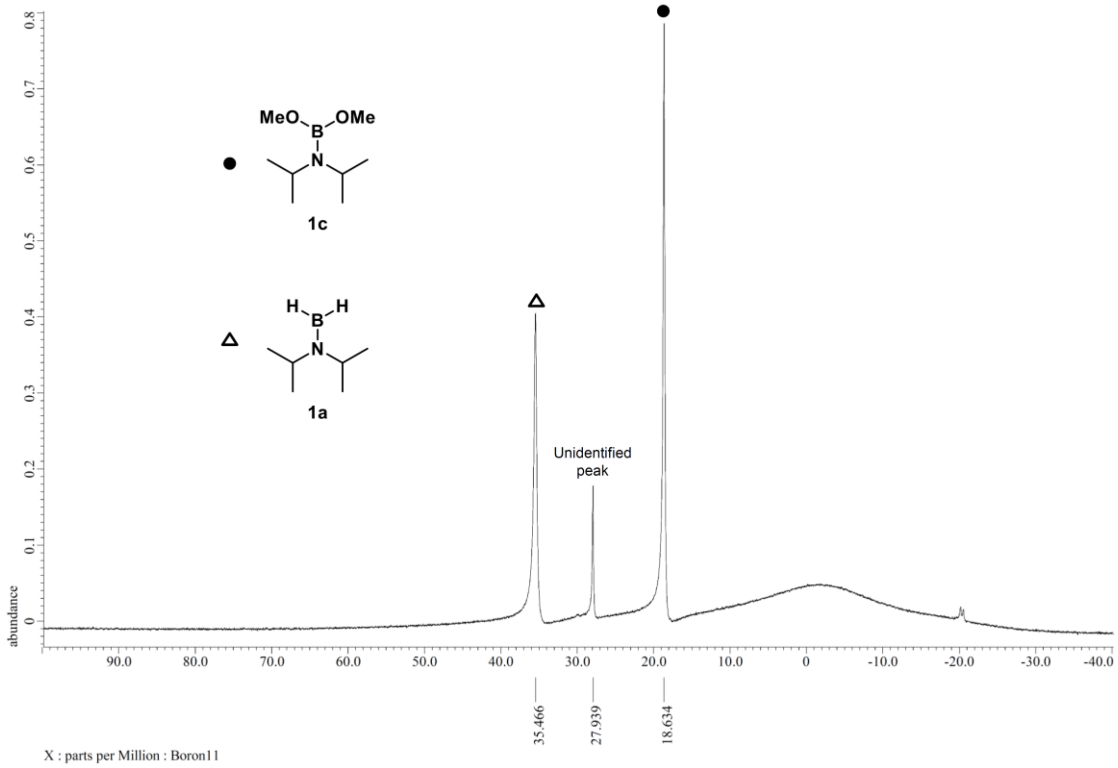
^{11}B NMR (toluene-d_8, 128.27 MHz): δ 18.6.



^{1}H NMR of **1c** in toluene-d_8

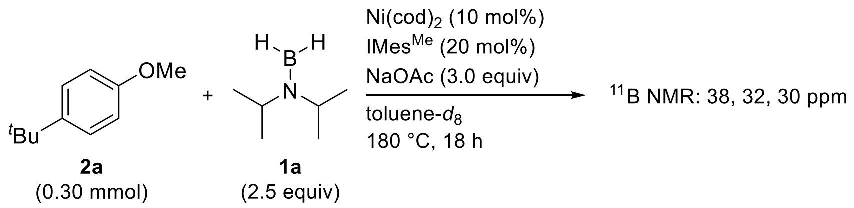


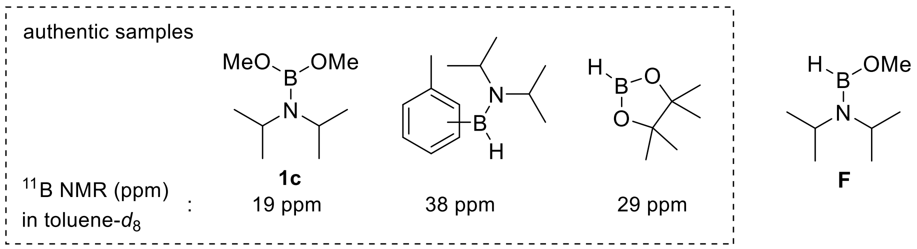
^{13}C NMR of **1c** in toluene-d_8



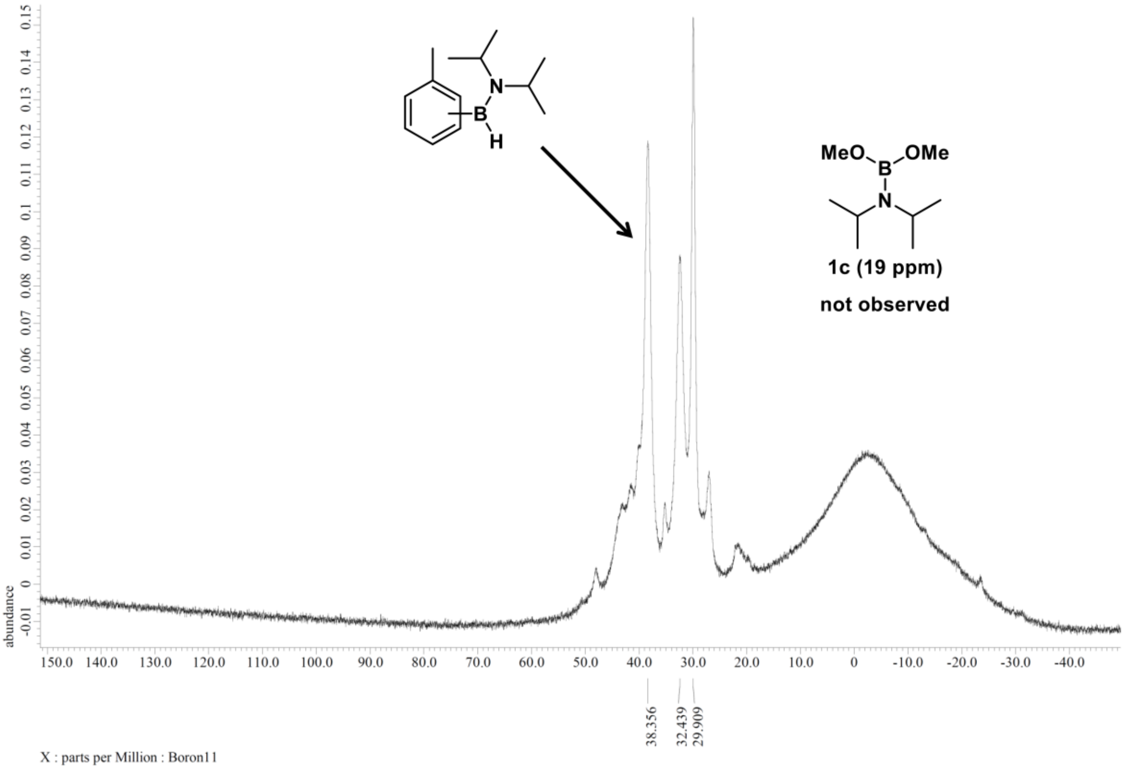
^{11}B NMR of **1c** in toluene-d_8

3.4.11 The Observation by ^{11}B NMR Spectroscopy after the Reaction



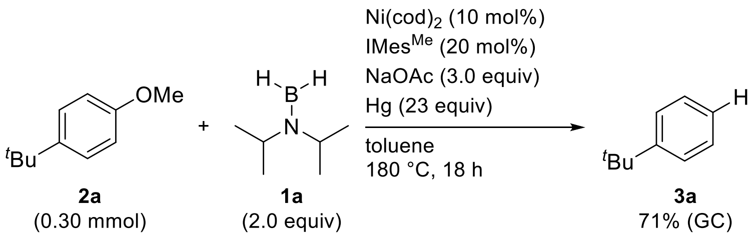


In a glovebox filled with nitrogen, Ni(cod)$_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), IMes^{Me} (20 mg, 0.060 mmol, 0.20 equiv) and toluene-d_8 (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv), **2a** (49 mg, 0.30 mmol, 1.0 equiv), and **1a** (85 mg, 0.75 mmol, 2.0 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 180 °C for 18 h. After the reaction mixture was cooled to room temperature, the NMR sample was prepared in a glovebox with N_2, and analyzed by ^{11}B NMR. Large signals were appeared at 38, 32 and 30 ppm in toluene-d_8. This result indicates that **1c** was not thought to be generated in this reaction, since we confirmed that the ^{11}B chemical shift of **1c** appeared at 19 ppm by separately synthesizing **1c**. We have already reported that the chemical shift corresponding to aminoborylated toluene compounds appeared at 38 ppm.[18] However, we could not assign the two signals appeared at 32 and 30 ppm. We expect that either signal probably corresponds to mono-methoxyaminoborane (**F**), since the chemical shift corresponding to HBpin appears at 29 ppm. These results indicates that **F** is incapable of reducing anisole and only one of two B-H bonds in **1a** reacts in this deoxygenated reaction.



^{11}B NMR of the reaction mixture observed in toluene-d_8 after the reaction

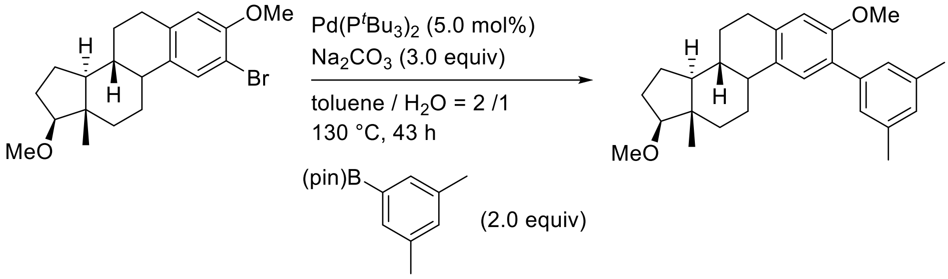
3.4.12 Hg Poisoning Test



In a glovebox filled with nitrogen, $Ni(cod)_2$ (8.3 mg, 0.030 mmol, 0.10 equiv), IMes^{Me} (20 mg, 0.060 mmol, 0.20 equiv) and toluene (1.0 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap, and stirred for 3 min at room temperature. NaOAc (74 mg, 0.90 mmol, 3.0 equiv), **2a** (49 mg, 0.30 mmol, 1.0 equiv), **1a** (68 mg, 0.60 mmol, 2.0 equiv) and Hg (1.4 g, 6.9 mmol, 23 equiv) were then added, and the cap was applied to seal the vial. The vial was stirred at 180 °C for 18 h. After the reaction mixture was cooled to room temperature, the crude mixture was filtered through silica gel eluting with EtOAc. The filtrate was analyzed by GC using eicosane as an internal standard. The yield was determined by GC analysis due to volatility of the product. GC yield of **3a** was 71%. This result indicates that a homogeneous catalyst is responsible for this reaction.

3.4.13 Synthetic Applications

(8*R*,13*S*,14*S*,17*S*)-2-(3,5-Dimethylphenyl)-3,17-Dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene.



Pd(P^{t}Bu$_3$)$_2$ (10 mg, 0.020 mmol, 0.050 equiv), 2-(3,5-dimethylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (184 mg, 0.79 mmol, 2.0 equiv), Na_2CO_3 (126 mg, 1.2 mmol, 3.0 equiv) and H_2O (0.70 mL) were added to a solution of (8*R*,13*S*,14*S*,17*S*)-2-bromo-3,17-dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene[40] (150 mg, 0.40 mmol, 1.0 equiv) in toluene (1.4 mL) in a 190 mL-sample vial with a Teflon sealed screwcap, and then the suspension was stirred at 130 °C for 43 h. After cooling to room temperature, H_2O (20 mL) was added to the reaction mixture. The resulting mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried over $MgSO_4$. The solvent was then removed under reduced pressure, and purified by flash column chromatography over silica gel eluting with hexane/EtOAc (10/1). The filtrate was concentrated in vacuo to give an arylated product as a white solid (141 mg, 88%).

R_f 0.37 (hexane/EtOAc = 1/1). Mp = 134 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.79 (s, 3H), 1.18-1.25 (m, 1H), 1.30-1.43 (m, 3H), 1.45-1.58 (m, 3H), 1.65-1.73 (m, 1H), 1.87-1.93 (m, 1H), 2.00-2.11 (m, 2H), 2.19-2.25 (m, 1H), 2.28-2.34 (m, 7H), 2.84-2.97 (m, 2H), 3.31 (t, *J* = 8.4 Hz, 1H), 3.37 (s, 3H), 3.76 (s, 3H), 6.67 (s, 1H), 6.94 (s, 1H), 7.09 (s, 2H), 7.19 (s, 1H).

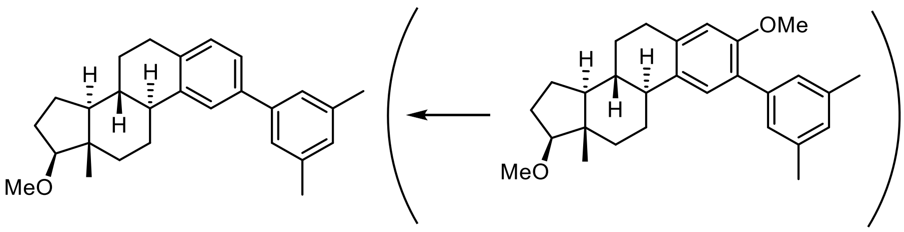
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 11.7, 21.6, 23.2, 26.6, 27.5, 27.9, 30.0, 38.2, 38.8, 43.4, 44.1, 50.4, 55.8, 58.1, 90.9, 111.6, 127.5, 128.2, 128.6, 128.7, 132.6, 137.1, 137.5, 138.9, 154.4.

IR (ATR): 2924 m, 1603 m, 1503 m, 1461 m, 1396 m, 1312 m, 1246 s, 1204 m, 1127 s, 1106 s, 1070 m, 1028 s, 889 m, 851 s, 790 w, 708 s.

MS m/z (% relative intensity): 405 (30), 404 (M^+, 100), 331 (10).

HRMS (EI): Calcd for $C_{28}H_{36}O_2$ 404.2715, Found 404.2712.

(8*R*,9*S*,13*S*,14*S*,17*S*)-2-(3,5-Dimethylphenyl)-17-methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene (6).



The typical procedure was followed using the corresponding aryl ether, and the reaction temperature was 180 °C.

R_f 0.40 (hexane/EtOAc = 10/1). White solid (66 mg, 59%). Mp = 129 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.81 (s, 3H), 1.16-1.28 (m, 2H), 1.31-1.52 (m, 4H), 1.58-1.63 (m, 1H), 1.65-1.76 (m, 1H), 1.89-1.95 (m, 1H), 2.02-2.13 (m, 2H), 2.27-2.35 (m, 1H), 2.37 (s, 6H), 2.39-2.45 (m, 1H), 2.89-2.92 (m, 2H), 3.33 (t, J = 8.2 Hz, 1H), 3.39 (s, 3H), 6.97 (s, 1H), 7.13 (d, J = 8.1 Hz, 1H), 7.17 (s, 2H), 7.32 (dd, J = 0.92, 8.1 Hz, 1H), 7.50 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 11.7, 21.6, 23.2, 26.4, 27.4, 27.9, 29.4, 38.2, 38.6, 43.3, 44.7, 50.6, 58.1, 90.9, 124.4, 124.6, 125.2, 128.7, 129.4, 135.9, 138.3, 139.1, 140.7, 141.9.

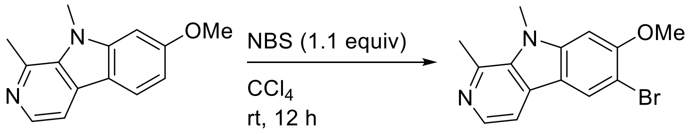
IR (ATR): 2926 s, 2361 w, 1601 m, 1455 m, 1379 m, 1105 s, 847 m, 790 m, 702 m.

MS m/z (% relative intensity): 375 (29), 374 (M^+, 100), 301 (32), 198 (17), 197 (100), 196 (11), 144 (25), 143 (17), 142 (17), 141 (14), 129 (21), 128 (14), 117 (25), 115 (11).

HRMS (EI): Calcd for $C_{27}H_{34}O$ 374.2610, Found 374.2606.

$[\alpha]_D^{20}$ = -33.4 (c = 5.8 × 10^{-2}, $CHCl_3$).

6-Bromo-7-methoxy-1,9-dimethyl-9*H*-pyrido[3,4-*b*]indole.



NBS (1.5 g, 8.4 mmol, 1.1 equiv) was added to a solution of **2av**[41] (1.8 g, 7.8 mmol, 1.0 equiv) in CH_2Cl_2 (70 mL), and then the resulting mixture was stirred at room temperature for 12 h while protected from light. After the reaction, H_2O (50 mL) was added, and then the mixture was extracted with CH_2Cl_2 (50 mL × 3). The combined organic extracts were washed with brine (50 mL) and dried over Na_2SO_4. The solvent was then removed under reduced pressure to give the crude product, which was purified by flash column chromatography over NH silica gel eluting with hexane/EtOAc (1/1) to give a mixture of a brominated product and succinimide. The mixture was dissolved in CH_2Cl_2, and then washed with 1 M NaOH (30 mL × 3). The separated organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure to give a brominated product as a pale yellow solid (1.9 g, 80%).

R_f 0.34 (NH silica, hexane/EtOAc = 1/1). Mp = 215 °C.

^{1}H NMR ($CDCl_3$, 600.13 MHz): δ 3.00 (s, 3H), 3.99 (s, 6H), 6.71 (s, 1H), 7.60 (d, J = 3.4 Hz, 1H), 8.13 (s, 1H), 8.26 (d, J = 3.4 Hz, 1H).

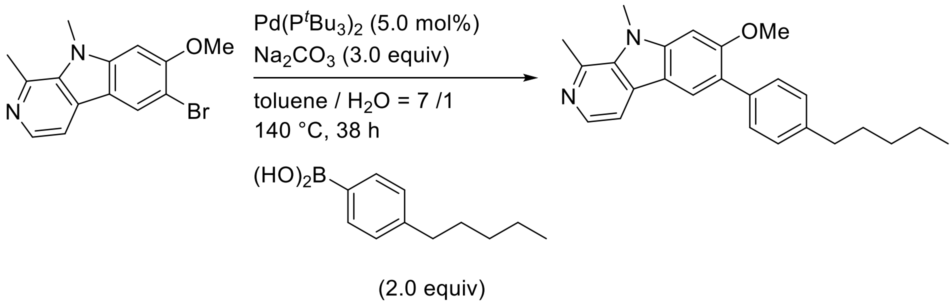
^{13}C NMR ($CDCl_3$, 150.92 MHz): δ 23.6, 32.5, 56.6, 92.3, 104.2, 112.3, 115.6, 125.6, 128.0, 135.9, 138.6, 141.4, 142.4, 156.4.

IR (ATR): 2937 w, 2360 w, 1623 m, 1563 m, 1489 w, 1447 s, 1399 m, 1362 m, 1327 m, 1282 w, 1241 s, 1136 m, 1106 m, 1037 s, 975 m, 894 w, 879 w, 825 s, 804 m, 714 m.

MS m/z (% relative intensity): 307 (15), 306 (96), 305 (31), 304 (100), 303 (15), 263 (23), 261 (23), 210 (24), 195 (10), 182 (10).

HRMS (EI): Calcd for $C_{14}H_{13}BrN_2O$ 304.0211, Found 304.0217.

7-Methoxy-1,9-dimethyl-6-(4-pentylphenyl)-9*H*-pyrido[3,4-*b*]indole.



Pd(P^{t}Bu$_3$)$_2$ (34 mg, 0.066 mmol, 0.050 equiv), (4-pentylphenyl)boronic acid (507 mg, 2.6 mmol, 2.0 equiv), Na_2CO_3 (420 mg, 4.0 mmol, 3.0 equiv) and H_2O (1.0 mL) were added to a solution of 6-bromo-7-methoxy-1,9-dimethyl-9*H*-pyrido[3,4-*b*]indole (400 mg, 1.3 mmol, 1.0 equiv) in toluene (7.0 mL) in a 190 mL-sample vial with a Teflon sealed screwcap, and then the suspension was stirred at 140 °C for 38 h. After cooling to room temperature, H_2O (30 mL) was added to the reaction mixture. The resulting mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried over $MgSO_4$. The solvent was then removed under reduced pressure, and purified by flash column chromatography over NH silica gel eluting with hexane/EtOAc (1/1). The filtrate was concentrated in vacuo to give an arylated product as a pale yellow solid (418 mg, 85%).

R_f 0.20 (NH silica, hexane/EtOAc = 1/1). Mp = 167 °C.

^{1}H NMR (CDCl$_3$, 399.78 MHz): δ 0.91-0.94 (m, 3H), 1.37-1.40 (m, 4H), 1.65-1.72 (m, 2H), 2.66 (t, *J* = 8.2 Hz, 2H), 3.08 (s, 3H), 3.96 (s, 3H), 4.13 (s, 3H), 6.89 (s, 1H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.51 (d, *J* = 7.8 Hz, 2H), 7.72 (d, *J* = 5.2 Hz, 1H), 7.98 (s, 1H), 8.27 (d, *J* = 5.2 Hz, 1H).

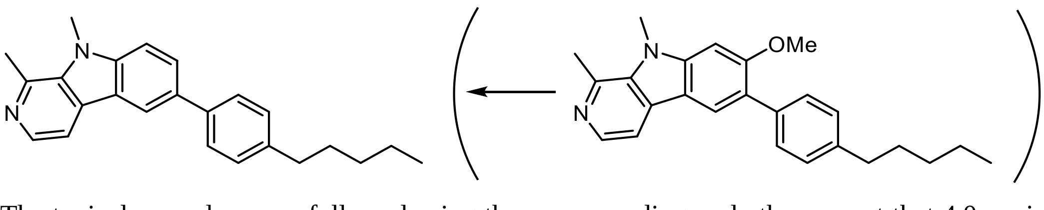
^{13}C NMR (CDCl$_3$, 100.53 MHz): δ 14.2, 22.0, 22.7, 31.3, 31.7, 32.5, 35.8, 56.0, 91.3, 112.5, 114.0, 123.5, 125.7, 128.2, 129.6, 130.3, 135.4, 135.6, 135.7, 139.8, 141.7, 143.6, 159.0.

IR (ATR): 2926 w, 2852 w, 2504 w, 1967 w, 1627 s, 1563 w, 1492 w, 1452 s, 1400 m, 1366 m, 1332 w, 1243 s, 1221 s, 1185 m, 1137 m, 1105 w, 1037 m, 958 w, 895 w, 826 s, 802 m, 722 m, 673 w.

MS m/z (% relative intensity): 373 (29), 372 (M^+, 100), 316 (11), 315 (46), 299 (13).

HRMS (EI): Calcd for $C_{25}H_{28}N_2O$ 372.2202, Found 372.2202.

6-(4-Pentylphenyl)-1,9-dimethyl-9*H*-pyrido[3,4-*b*]indole (7).



The typical procedure was followed using the corresponding aryl ether except that 4.0 equiv of **1a** was used, and that the reaction temperature was 180 °C.

R_f 0.31 (NH silica, hexane/EtOAc = 1/1). Pale yellow solid (72 mg, 70%). Mp = 94 °C.

^{1}H NMR (CDCl$_3$, 399.78 MHz): δ 0.90-0.94 (m, 3H), 1.33-1.39 (m, 4H), 1.64-1.72 (m, 2H), 2.67 (t, *J* = 7.8 Hz, 2H), 3.10 (s, 3H), 4.16 (s, 3H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 1H), 7.62 (d, *J* = 6.4 Hz, 2H), 7.82-7.86 (m, 2H), 8.29 (d, *J* = 1.4 Hz, 1H), 8.32 (d, *J* = 5.5 Hz, 1H).

^{13}C NMR (CDCl$_3$, 100.53 MHz): δ 14.2, 22.7, 23.8, 31.4, 31.7, 32.5, 35.7, 109.8, 113.1, 119.7, 121.7, 127.2, 127.8, 129.0, 129.1, 133.2, 136.4, 138.3, 138.9, 141.5, 141.7, 142.0.

IR (ATR): 2954 m, 2925 s, 2855 m, 1626 m, 1567 m, 1461 s, 1398 w, 1377 m, 1360 m, 1300 m, 1240 m, 1142 w, 1106 m, 1046 w, 984 m, 814 s, 795 s, 671 m.

MS m/z (% relative intensity): 343 (29), 342 (M^+, 100), 286 (17), 285 (70).

HRMS (EI): Calcd for $C_{24}H_{26}N_2$ 342.2096, Found 342.2101.

3.5 References

(1) Selected examples: (a) Arnott, G.; Brice, H.; Clayden, J.; Blaney, E. *Org. Lett.* **2008**, *10*, 3089. (b) Rohbogner, C. J.; Clososki, G. C.; Knochel, P. *Angew. Chem. Int. Ed.* **2008**, *47*, 1503.

(2) A review on *ortho* lithiation with a methoxy group: Snieckus, V. *Chem. Rev.* **1990**, *90*, 879. Selected recently reported examples: (a) Hansen, M. J.; Lerch, M. M.; Szymanski, W.; Feringa, B. L. *Angew. Chem. Int. Ed.* **2016**, *55*, 13514. (b) Xiong, X.; Zhu, R.; Huang, L.; Chang, S.; Huang, J. *Synlett* **2017**, *28*, 2046. (c) Slocum, D. W.; Maulden, E. A.; Whitley, P. E.; Reinscheld, T. K.; Jackson, C. S.; Maddox, J. B. *Eur. J. Org. Chem.* **2017**, 6882. (d) Reddy, L. R.; Kotturi, S.; Waman, Y.; Patel, C.; Patwa, A.; Shenoy, R. *Chem. Commun.* **2018**, *54*, 7007.

(3) (a) Oyamada, J.; Nishiura, M.; Hou, Z. *Angew. Chem. Int. Ed.* **2011**, *50*, 10720. (b) Oyamada, J.; Hou, Z. *Angew. Chem. Int. Ed.* **2012**, *51*, 12828. (c) Shi, X.; Nishiura, M.; Hou, Z. *J. Am. Chem. Soc.* **2016**, *138*, 6147. (d) Yamamoto, A.; Nishiura, M.; Oyamada, J.; Koshino, H.; Hou, Z. *Maclomolecules* **2016**, *49*, 2458. (e) Yamamoto, A.; Nishiura, M.; Yang, Y.; Hou, Z. *Organometallics* **2017**, *36*, 4635. (f) Xue, C.; Luo, Y.; Teng, H.; Ma, Y.; Nishiura, M.; Hou, Z. *ACS Catal.* **2018**, *8*, 5017.

(4) (a) Brasche, G.; García-Fortanet, J.; Buchwald, S. L. *Org. Lett.* **2008**, *10*, 2207. (b) Ciana, C.-L.; Phipps, R. J.; Brandt, J. R.; Meyer, F.-M.; Gaunt, M.-J. *Angew. Chem. Int. Ed.* **2011**, *50*, 458. (c) Berzina, B.; Sokolovs, I.; Suna, E. *ACS Catal.* **2015**, *5*, 7008.

(5) *Ipso*-substitution of anisole derivatives by photoredox catalysis: Tay, N. E. S.; Nicewicz, D. A. *J. Am. Chem. Soc.* **2017**, *139*, 16100.

(6) Reviews on the Ni-catalyzed cleavage reactions of C(aryl)-O bonds: (a) Yu, D.-G.; Li, B.-J.; Shi, Z.-J. *Acc. Chem. Res.* **2010**, *43*, 1486. (b) Li, B.-J.; Yu, D.-G.; Sun, C.-L.; Shi, Z.-J. *Chem. Eur. J.* **2011**, *17*, 1728. (c) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. *Chem. Rev.* **2011**, *111*, 1346. (d) Tobisu, M.; Chatani, N. *Top. Organomet. Chem.* **2013**, *44*, 35. (e) Yamaguchi, J.; Muto, K.; Itami, K. *Eur. J. Org. Chem.* **2013**, 19. (f) Cornella, J.; Zarate, C.; Martin, R. *Chem. Soc. Rev.* **2014**, *43*, 8081. (g) Tobisu, M.; Chatani, N. *Acc. Chem. Res.* **2015**, *48*, 1717.

(7) (a) Álvarez-Bercedo, P.; Martin, R. *J. Am. Chem. Soc.* **2010**, *132*, 17352. (b) Tobisu, M.; Yamakawa, K.; Shimasaki, T.; Chatani, N. *Chem. Commun.* **2011**, *47*, 2946. (c) Sergeev, A. G.; Hartwig, J. F. *Science* **2011**, *332*, 439. (d) Tobisu, M.; Morioka, T.; Ohtsuki, A.; Chatani, N. *Chem. Sci.* **2015**, *6*, 3410. (e) Wiensch, E. M.; Todd, D. P.; Montgomery, J. *ACS Catal.* **2017**, *7*, 5568. (f) Xi, X.; Chen, T.; Zhang, J.-S.; Han, L.-B. *Chem. Commun.* **2018**, *54*, 1521.

(8) Several heterogeneous systems for reductive cleavage of anisole derivatives have also been reported: (a) Ren, Y.; Yan, M.; Wang, J.; Zhang, Z. C.; Yao, K. *Angew. Chem. Int. Ed.* **2013**, *52*, 12674. (b) Ren, Y.-L.; Tian, M.; Tian, X.-Z.; Wang, Q.; Shang, H.; Wang, J.; Zhang, Z. C. *Catal. Commun.* **2014**, *52*, 36.

(9) Lewis acid additives often promote transition-metal-catalyzed activation of inert bonds. Selected examples: (a) Nakao, Y. *Bull. Chem. Soc. Jpn.* **2012**, *85*, 731. (b) Guan, W.; Zeng, G.; Kameo, H.; Nakao, Y.; Sakaki, S. *Chem. Rec.* **2016**, *16*, 2405.

(10) A review on catalytic reduction of amides: Volkov, A.; Tinnis, F.; Slagbrand, T.; Trillo, P.; Adolfsson, H. *Chem. Soc. Rev.* **2016**, *45*, 6685.

(11) (a) Ru-catalyzed Suzuki-Miyaura type reaction of C-O bonds at the β-positions has been reported: Ogiwara, Y.; Kochi, T.; Kakiuchi, F. *Org. Lett.* **2011**, *13*, 3254. (b) Fe-catalyzed Kumada-Tamao-Corriu type reaction of C-O bonds at the β-positions has been reported: Luo, S.; Yu, D.-G.; Zhu, R.-Y.; Wang, X.; Wang, L.; Shi, Z.-J. *Chem. Commun.* **2013**, *49*, 7794.

(12) Reviews on reductive reactions using borane derivatives: (a) *Advanced Organic Chemistry Part B: Reactions and Synthesis, Fifth Edition* (Eds.: Carey, F. A.; Sundberg, R. J.), Springer **2008**. (b) Chong, C. C.; Kinjo, R. *ACS Catal.* **2015**, *5*, 3238.

(13) (a) Beck, R.; Shoshani, M.; Johnson, S. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 11753. (b) Tobisu, M.; Nakamura, K.; Chatani, N. *J. Am. Chem. Soc.* **2014**, *136*, 5587.

(14) Crestani, M. G.; Muñoz-Hernández, M.; Arévalo, A.; Acosta-Ramírez, A.; García, J. J. *J. Am. Chem. Soc.* **2005**, *127*, 18066.

(15) (a) Furukawa, T.; Tobisu, M.; Chatani, N. *Chem. Commun.* **2015**, *51*, 6508. (b) Zhang, H.; Hagihara, S.; Itami, K. *Chem. Lett.* **2015**, *44*, 779.

(16) (a) Sergeev, A. G.; Webb, J. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2012**, *134*, 20226. (b) Gao, F.; Webb, J. D.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2016**, *55*, 1474.

(17) Crabtree, R. H. *Chem. Rev.* **2012**, *112*, 1536.

(18) Tobisu, M.; Igarashi, T.; Chatani, N. *Beilstein J. Org. Chem.* **2016**, *12*, 654.

(19) Kinura, H.; Tobisu, M.; Chatani, N. *J. Am. Chem. Soc.* **2015**, *137*, 1593.

(20) Bantreil, X.; Nolan, S. P. *Nat. Protoc.* **2011**, *6*, 69.

(21) Schwarzer, M.; Konno, R.; Hojo, T.; Ohtsuki, A.; Nakamura, K.; Yasutome, A.; Takahashi, H.; Shimasaki, T.; Tobisu, M.; Chatani, N.; Mori, S. *J. Am. Chem. Soc.* **2017**, *139*, 10347.

(22) Matsumoto, K.; Yoshida, M.; Shindo, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 5272.

(23) Dash, P.; Janni, M.; Peruncheralathan, S. *Eur. J. Org. Chem.* **2012**, 4914.

(24) Clayden, J.; Tchabanenko, K.; Yasin, S. A.; Turnbull, M. D. *Synlett* **2001**, *2*, 302.

(25) Uemura, T.; Igarashi, T.; Noguchi, M.; Shibata, K.; Chatani, N. *Chem. Lett*. **2015**, *44*, 621.

(26) Tobisu, M.; Takahira, T.; Ohtsuki, A.; Chatani, N. *Org. Lett.* **2015**, *17*, 680.

(27) Barbasiewicz, M.; Szadkowska, A.; Makal, A.; Jarzembska, K.; Wozniak, K.; Grela, K. *Chem. Eur. J.* **2008**, *14*, 9330.

(28) Naidu, A. B.; Jaseer, E. A.; Sekar, G. *J. Org. Chem.* **2009**, *74*, 3675.

(29) Bindal, R. D.; Katzenellenbogen, J. A. *J. Org. Chem.* **1987**, *52*, 3181.

(30) Liu, X.; Hsiao, C.-C.; Kalvet, I.; Leiendecker, M.; Guo, L.; Schoenebeck, F.; Rueping, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 6093.

(31) Johnson, S. M.; Connelly, S.; Wilson, I. A.; Kelly, J. W. *J. Med. Chem.* **2008**, *51*, 6348.

(32) Nakamura, K.; Tobisu, M.; Chatani, N. *Org. Lett.* **2015**, *17*, 6142.

(33) Bubniene. G.; Malinauskas, T.; Daskeviciene, M.; Jankauskas, V.; Getautis, V. *Tetrahedron* **2010**, *66*, 3199.

(34) Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2011**, *133*, 389.

(35) Muñoz-Muñiz, O.; Juaristi, E. *Tetrahedron Lett.* **2003**, *44*, 2023.

(36) Tobisu, M.; Yasutome, A.; Kinuta, H.; Nakamura, K.; Chatani, N. *Org. Lett.* **2014**, *16*, 5572.

(37) Chua, Y.-Y.; Duong, H. A. *Chem. Commun.* **2014**, *50*, 8424.

(38) Tobisu, M.; Takahira, T.; Chatani, N. *Org. Lett.* **2015**, *17*, 4352.

(39) Budén, M. E.; Guastavino, J. F.; Rossi, R. A. *Org. Lett.* **2013**, *15*, 1174.

(40) Liu, J.-H.; Yanf, C.-T.; Lu, X.-Y.; Zhang, Z.-Q.; Xu, L.; Cui, M.; Lu, X.; Xiao, B.; Fu, Y.; Liu, L. *Chem. Eur. J*. **2014**, *20*, 15334.

(41) Bálint, B.; Wéber, C.; Cruzalegui, F.; Burbridge, M.; Kotschy, A. *ChemMedChem* **2017**, *12*, 932.

Conclusion

The research reported in this thesis was directed at new types of catalytic reactions using diisopropylaminoborane.

In Chapter 1, the Ir-catalyzed borylation reaction of aromatic C-H bonds using diisopropylaminoborane as a borylating reagent is described. The use of an NHC ligand is essential for an efficient reaction. This reaction can be applied to a series of heterocycles and benzene derivatives. The resulting aminoborylated intermediates are converted into various boron products by the treatment with protecting reagents in a one-pot reaction. The development of this reaction using an aminoborane reagent enabled the synthesis of boron compounds bearing various protecting groups just by one catalytic system.

In Chapter 2, the Pd-catalyzed two-fold borylation of dihalides using diisopropylaminoborane for the synthesis of cyclic diarylborinic acids is described. Although no catalytic reaction using both of two B-H bonds of an aminoborane reagent have been reported even in the presence of an excess amount of aryl halides, in this reaction of dihalides, the difficult second borylation is an intramolecular process, which promotes this process to give cyclic diarylborinic acids efficiently. Diaryborinic acids can be used in annulative two-fold Suzuki-Miyaura cross coupling reactions with dihalides to afford a series of unique π-conjugated molecules.

In Chapter 3, the Ni-catalyzed reductive cleavage of aromatic C-O bonds in anisole derivatives using diisopropylaminobornae as a boron source is described. Unlike previously reported methods, this reaction can reduce not only naphthyl or polyaromatic ethers but also monoaromatic ethers by the higher Lewis acidity of diisopropylaminoborane than other hydroborane reagents. This reaction allows methoxy groups to serve as tracelss *ortho*-directing groups, which will provide opportunities for the late-stage functionalization of anisole derivatives.

In this study, the utility of diisopropylaminoborane can be expanded through the development of the above three catalytic reactions. All these reactions proceed by taking advantage of characteristic properties of an aminoborane reagent: 1) two B-H bonds 2) high Lewis acidity. The knowledge and findings obtained through this study will contribute to the further development of catalytic reactions using an aminoborane reagent. Especially, two B-H bonds of an aminoborane reagent will be utilized frequently in the future like a dihydrosilane reagent in catalytic reactions.

List of Publications

(1) Iridium/N-Heterocyclic Carbene-Catalyzed C-H Borylation of Arenes Using Diisopropylaminoborane
Mamoru Tobisu, Takuya Igarashi and Naoto Chatani
Beilstein J. Org. Chem. **2016**, *12*, 654-661.

(2) Catalytic Double Carbon-Boron Bond Formation for the Synthesis of Cyclic Diarylborinic Acids as Versatile Building Blocks for π-Extended Heteroarenes
Takuya Igarashi, Mamoru Tobisu and Naoto Chatani
Angew. Chem. Int. Ed. **2017**, *56*, 2069-2073.

(3) Nickel-Catalyzed Reductive Cleavage of Carbon-Oxygen Bonds in Anisole Derivatives Using Diisopropylaminoborane
Takuya Igarashi, Akira Haito, Naoto Chatani and Mamoru Tobisu
ACS Catal. **2018**, *8*, 7475-7483.

Supplementary List of Publications

(1) $Pd(OAc)_2$-Catalyzed Lactonization of Arylacetamides Involving Oxidation of C-H Bonds
Takeshi Uemura, Takuya Igarashi, Moe Noguchi, Kaname Shibata and Naoto Chatani
Chem. Lett. **2015**, *44*, 621-623.

(2) Construction of Mouse-Embryonic-Cell Derived 3D-Pacemaker Tissues by Layer-by-Layer Nanofilm Coating
Yuto Amano, Takuya Igarashi, Akihiro Nishiguchi, Michiya Matsusaki, Yukihiro Saito, Kazufumi Nakamura, Hiroshi Ito and Mitsuru Akashi
ChemNanoMat **2016**, *5*, 466-471.

(3) Nickel-Catalyzed Borylation of Aryl and Benzyl 2-Pyridyl Ethers: A Method for Converting a Robust *ortho*-Directing Group
Mamoru Tobisu, Jiangning Zhao, Hirotaka Kinuta, Takayuki Furukawa, Takuya Igarashi and Naoto Chatani
Adv. Synth. Catal. **2016**, *358*, 2417-2421.