博　士　論　文

Development of *ortho*-Selective C-H Borylation Reaction of Aromatic Compounds

(芳香族化合物オルト位選択的 C–H 結合ホウ素化反応の開発)

Li Hongliang

李 紅亮

Contents

Abbreviations

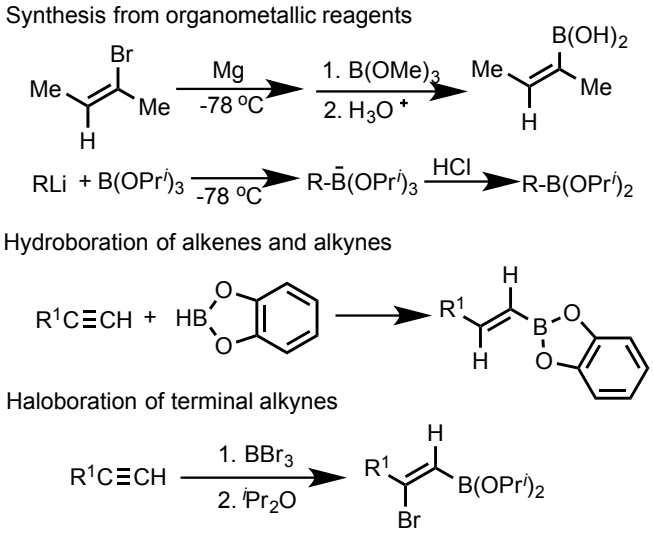
Ar	aryl
Ac	acyl
Bpin	pinacolate boryl
^{n}Bu	tert-butyl
cat.	Catalyst
cod	1,5-Cyclooctadiene
dtbpy	2,2'-dimethylbipyridine
DCM	dichloromethane
equiv	equivalent
ESI-Ms	electropspray ionization mass spectrometry
Et	ethyl
FG	functional group
h	hour
HRMS	high performance liquid chromate graphy
IR	infrared spectroscopy
L	ligand
m	*meta*
Me	methyl
MTBE	methyl *tert*-butyl ether
NMR	nuclear magnetic resonance

o	*ortho*
p	*para*
ph	phenyl
Pr	propyl
R	alkyl or general substituent
rt	room temperature
t	tertary
THF	tetrahedrofuran
Toyl	2-methylphenyl
Tol	toluene
X	unknown group

Chapter 1

Introduction

Carbon-Carbon bonds are the molecular "bricks and mortar" from which diverse architectures in living organisms and manmade materials are constructed. In the field of organic chemistry, there are numerous methods for carbon-carbon bond construction ranging from traditional nucleophilic reaction to metal catalyzed reaction [1]. Among of them, Suzuki-Miyaura reaction is one of the most powerful methods for the construction of C-C bonds since its discovery in 1979[2]. The use of an arylboron reagent and an organic halide or pseudo-halide in the presence of a transition metal catalyst such as palladium or nickel and a base is the standard condition of this reaction. In addition, organoboron reagents are extensively used as versatile intermediates in synthetic chemistry because it can be converted to more complex molecules by further transformations, such as Chan-Lam-Evans coupling[3] and oxidation[4]. Therefore, developing a highly effective method for synthesis of organoboron reagents is very desirable.

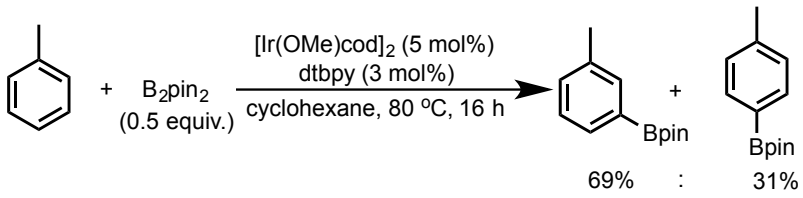


Scheme 1-1 Traditional methods for preparation of organoboron reagents

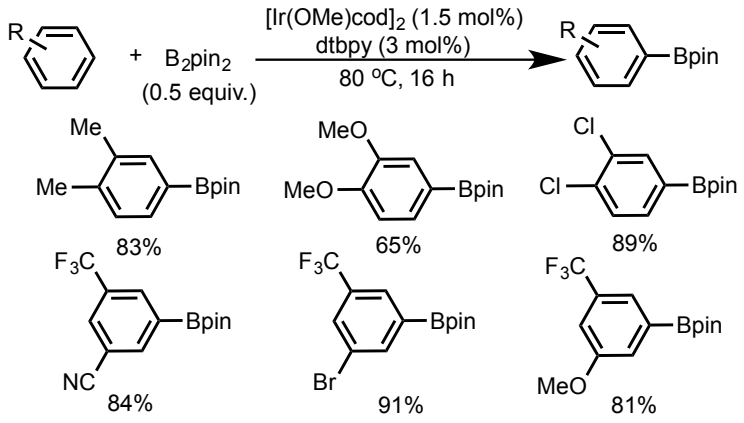
Traditional methods to obtain organoboron reagents are categorized to three main methods (**Scheme 1.1**), which contain synthesis from organolithium or organomagnesium, hydroboration of alkenes or alkynes and haloboration of terminal alkynes[5]. However, there are some limitations of these methods. For example, the synthesis from organometallics usually requires stoichiometric amounts of strong base such as *n*-BuLi and very lower temperature. As for the reactions of hydroboration and haloboration, the boron atom always adds to the terminal position of alkenes or alkynes. It is difficult to obtain internal boron reagents form these two methods. Besides, these three methods also are not necessarily in accordance with the rule of atomic economy.

The development of transition metal catalyzed C-H borylation provides a good way for preparation of organoboron reagents, especially for aromatic boron reagents. The most active catalyst for the borylation of aromatic compounds is the iridium/bipyridine catalytic system, which was found by Prof. Hartwig, Ishiyama, and Miyaura *et al*. in 2002 [6].

a) Borylation of *mono*-substituted arene



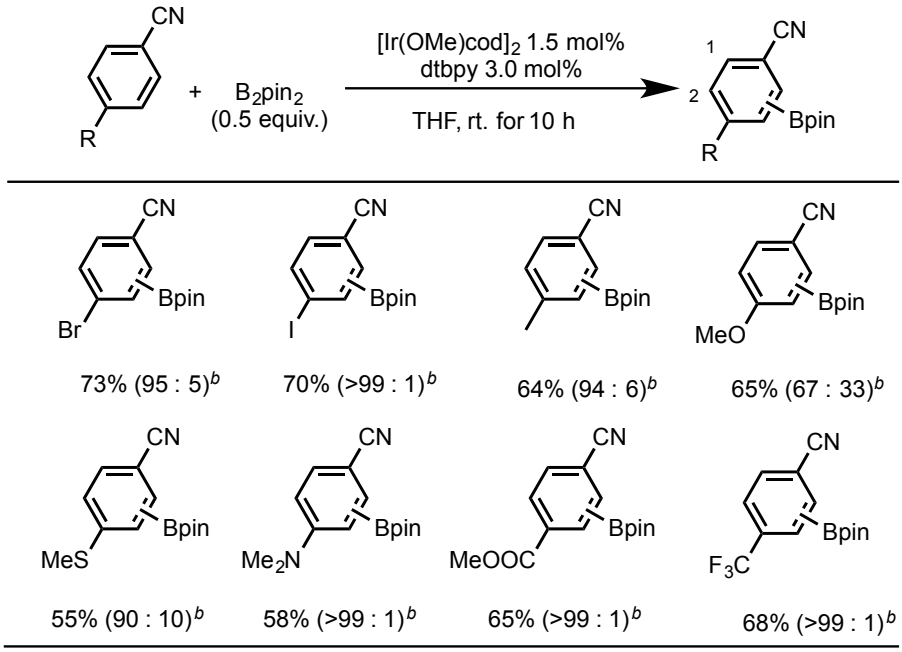
b) Borylation of *di*-substituted arene



Scheme 1-2 Steric effects on borylation of *mono*- and *di*-substituted arenes

Moreover, they also found that the C-H borylation reaction often occurs with regioselectivity which is controlled predominantly by steric effect[7]. For instance, for *mono*-substituted arenes as substrates, borylation always gives a mixture of *meta*- and *para*-borylated products in a 2 : 1 ratio[6]. Usually, the *ortho*-borylated isomer was not formed because of the steric hindrance of methyl substituent (**Scheme 1-2**, a)). In the case of *di*-substituted arenes, borylation reaction always proceeds at the position with less steric hindrance[8].

Reactions of 1,4-disustituted aromatic compounds could account for this steric effect more apparently. Borylation of symmetrically 1,4-disubstituted arenes will give rise to 1,2,4-trisubstituted products. For asymmetrically 1,4-substituted substrates, borylation regioselectively proceeds at the *ortho*-position of the substituent with less steric hindrance between the two possible reactive positions[9].



[a] Yields are for isolated products based on the limiting reagent
[b] Isomers(1 : 2) ratios were determined from crude reaction mixtures by GC integration

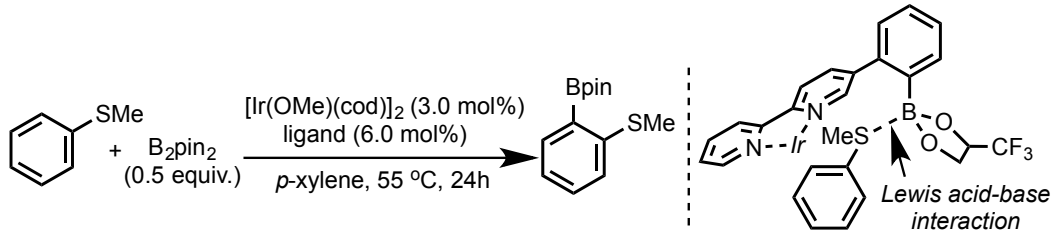
Scheme 1-3 Steric effect on borylation of 1,4-disubstituted arenes

In contrast, the regioselectivity of C-H borylation for heteroaromatic compounds is largely controlled by electronic effect. The five-membered ring heterocycles such as

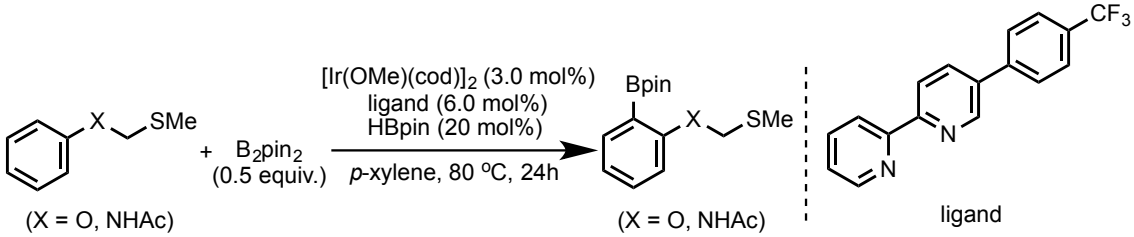
furan, thiophene or pyrrole give products with boryl group at alpha position to the heteroatom. Reactions of benzofuran, benzothiphene and indole also lead to borylation proceeded at alpha position to the heteroatom[10].

Although C-H borylation of aromatic compounds controlled by steric effect could lead to reactions occurred with regioselectivity, many challenges still exist in this kind of reaction. For example, the repulsion between substituent(s) of substrates and iridium/bipyridine catalytic species make it difficult to achieve *ortho*-selective C-H borylation of *mono*-substituted aromatic compounds. Therefore, the purpose of my research work during PhD stage is to develop a method which could overcome the steric effect to achieve *ortho*-selective C-H borylation of aromatic compounds.

a) The *ortho*-selective C-H borylation of aryl sulfides[11]



b) The *ortho*-selective C-H borylation of phenol and aniline derivatives



Scheme 1-4 Outline of my research works throughout my doctor course

In these three years, I developed two methods of *ortho*-selective C-H borylation of aromatic compounds. One is (1) Lewis acid-base interaction-controlled *ortho*-selective C-H borylation of aryl sulfides. The other is (2) Iridium/bipyridine catalyzed *ortho*-selective C-H borylation of phenol and aniline derivatives. In the following sections, I will describe the details of these two methods.

References

1. Cho, J.-Y.; Tse, M.-K.; Holmes, D.; Smith III, M. R. *Science* **2002**, *295*, 305.
2. Maluenda, I.; Navarro, S. *Molecules* **2015**, *20*, 7528.
3. a) Chan, D. M.; Monaco, K. L.; Wang, R. P.; Winteres, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933; b) Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett*. **1998**, *39*, 2937; c) Lam, Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M.; Combs, T. A. *Tetrahedron Lett.* **1998**, *39*, 2941.
4. For several examples, see: a) Simon, J.; Salzbrunn, S.; Prakash, G. K.; Petasis, N. A.; Olah, G. A. *J. Org. Chem.* **2001**, *66*, 633; b) Zhu, C.; Wang, R.; Falck, J. R. *Org. Lett.* **2012**, *14*, 3494; c) Kaewmati, P.; Somsook, E.; Dhital, N. R.; Sakurai, H. *Tetrahedron Lett.* **2012**, *53*, 6104; d) Chen, D.-S.; Huang, J.-M. *Synlett* **2013**, 499.
5. Miyaura, N.; Suzuki, A. *Chem. Rev.,* **1995**, *95*, 2457.
6. Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J.-F. *J. Am. Chem. Soc.* **2002**, *124*, 390.
7. a) Hartwig, J.-F. *Chem. Soc. Rev.* **2011**, *40*, 1992; b) Ros, A.; Fernandez, R.; Lassaletta, J. M. *Chem. Soc. Rev.* **2014**, *43*, 3229.
8. a) Ishiyama, T.; Takagi, J.; Hartwig, J.-F. and Miyaura, N. *Angew. Chem. Int. Ed.* **2002**, *41*, 3056; b) Ishiyama, T.; Nobuta, Y.; Hartwig, J.-F. and Miyaura, N. *Chem. Commun.,* **2003**, 2924.
9. Chotana, G. A.; Rak, M. A. and Smith III, R. *J. Am. Chem. Soc.* **2005**, *127*, 10539.
10. a) Takai, J.; Sato, K.; Hartwig, J.-F.; Ishiyama, T. and Miyaura, N. *Tetrahedron Lett*. **2002**, *43*, 5649; b) Ishiyama, T.; Takagi, J.; Yonekawa, Y.; Hartwig, J.-F. and Miyaura, N. *Adv. Synth. Catal.* **2003**, *345*, 1103.
11. Li, H.-L.; Kuninobu, Y.; Kanai, M. *Angew. Chem. Int. Ed.* **2017**, *56*, 1495.

Chapter 2

Development of *ortho*-Selective C-H Borylation of Aryl Sufides Controlled by Lewis Acid-Base Interaction

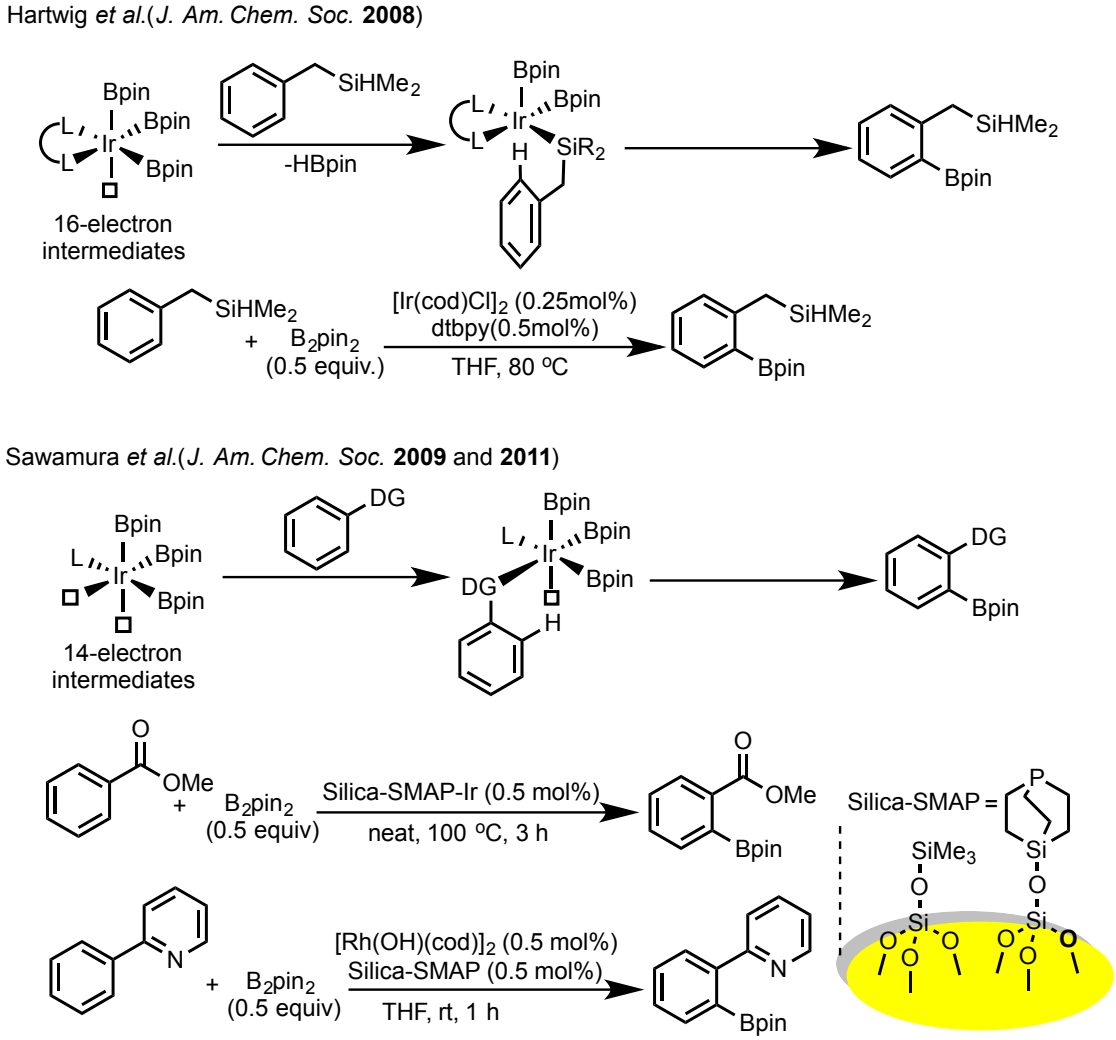
2.1 Introduction

C-H activation reactions have become a powerful method to direct functionalization of alkyl, alkenyl, and aryl C-H bonds over the past few decades. Among them, iridium catalyzed transformation of aryl C-H bonds to C-B bonds is one of the most useful methods. However, just like above description, a central challenge in these reactions is controlling their site selectivity, especially for *ortho*-selectivity, because steric effects often dominate the regioselectivity. Over the past decade, some methods have been developed to accomplish *ortho*-selective C-H borylation by catalysts or substrates modification[1]. Generally, these methods can be divided into the following three strategies including directing group (DG) assist, ligand-enabled and non-covalent bond interaction controlled *ortho*-selective C-H borylation.

2.1.1 Precedents of directing group assist *ortho*-selective C-H borylation

In this section, precedents of directing group assisted *ortho*-selective C-H borylation are briefly reviewed[2]. In 2008, Hartwig *et al*. disclosed the first example of *ortho*-selective C-H borylation for aromatic substrates directed by alkylhydrosilyl group. This reaction proceeded according to a relay directed process. The alkylhydrosilyl group could reversibly attach to iridium center by σ-bond metathesis process to form a 16-electron intermediate, and bring iridium-boryl catalytic species close to *ortho*-position, which will facilitate the cleavage of *ortho* C-H bond (**Scheme 2-1**). Benzyldimethylsilane as substrate, the reaction could proceed with high *ortho*-selectivity in good yield.

In 2009, Sawamura *et al*. reported an *ortho*-selective C-H borylation of aromatic compounds catalyzed by a silica supported *mono*-dentate phosphine ligand. In this reaction, *mono*-dentate ligand and iridium formed a 14-electron intermediate, which contains two vacant sites, one for directing group of substrate and the other for the cleavage of *ortho* C-H bond. Therefore, the *ortho*-selective C-H borylation proceeded through the intermediate. The reaction has very wide substrates scope including benzoate, ether, sulfonate and so on. In addition, he also developed an *ortho*-selective C-H borylation of 2-phenylpyridine in 2011, which was catalyzed by Rh with silica supported *mono*-dentate phosphine ligand.



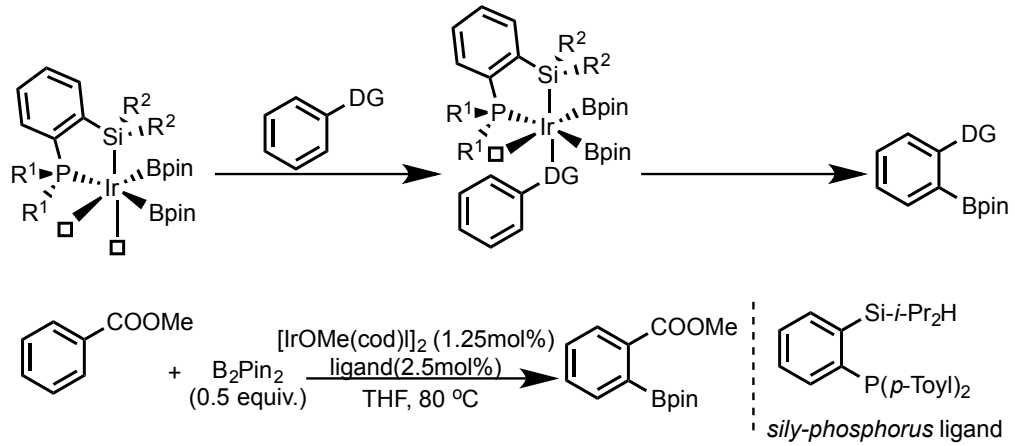
Scheme 2-1 Directing group assisted *ortho*-selective C-H borylation

2.1.2 Precedents of ligand-enabled *ortho*-selective C-H borylation

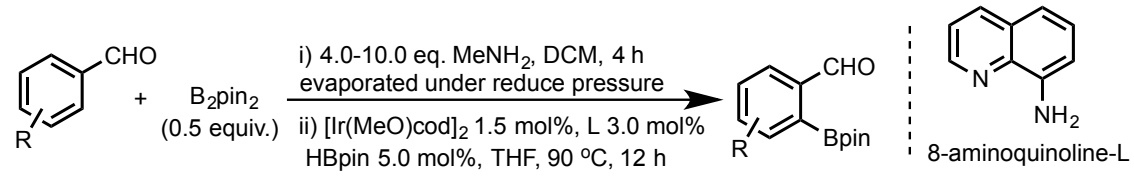
Ligand-enabled *ortho*-selective C-H borylation is as its name, in which *ortho*-selectivity is achieved by modifying ligand structure[3]. In traditional methods, bipyridine type ligand is the most commonly used ligand in iridium catalyzed sp^2 C-H borylation reaction. In 2014, Smith *et al*. reported silyl-phosphorous ligand catalyzed *ortho*-selective C-H borylation of alkyl benzoate. The reaction not only gave good yields of borylated product but also controlled *ortho*-selectivity very well.

In 2016, Chattopadhyay *et al*. developed *ortho*-selective C-H borylation of benzaldehydes. The *ortho*-borylation could be achieved using 8-aminoquinoline as ligand, in which methylamine was as the traceless protecting/directing group. The yield of *ortho*-borylated products could reach up to 80%.

Smith *et al.*(*J. Am. Chem. Soc.* **2014**)



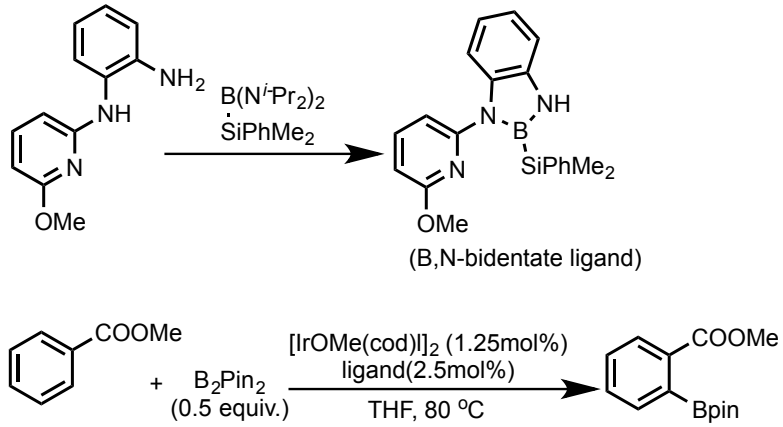
Chattopadhyay *et al.*(*J. Am. Chem. Soc.* **2016**)



Scheme 2-2 Ligand-enabled *ortho*-selective C-H borylation

In 2017, Li *et al*. reported a new *ortho*-selective C-H borylation catalyzed by a designed N,B-bidentate boryl ligand. By introducing convenient silylborane precursors onto N,B-bidentate boryl ligands, the iridium (III) complex was formed via Si-B oxidative addition. The *ortho*-borylation reaction could be suitable for a broad range of substrates.

Li *et al*.(*J. Am. Chem. Soc.* **2017**)



Scheme 2-3 B, N-bidentate ligand-enabled *ortho*-selective C-H borylation

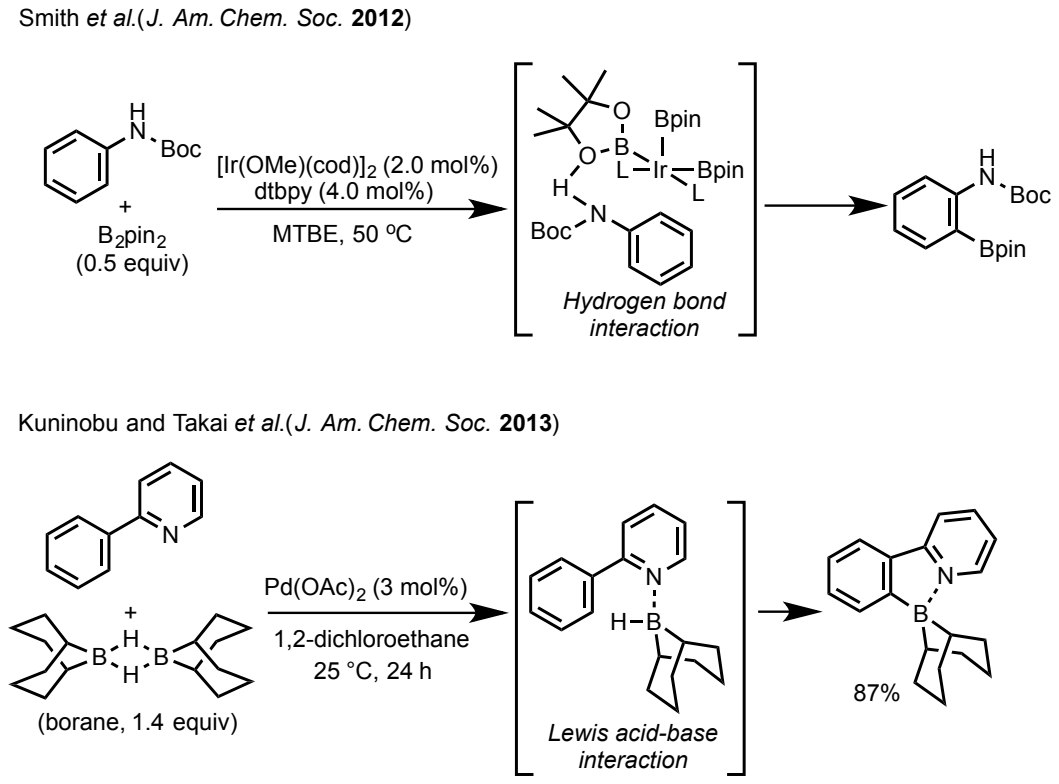
2.1.3 Precedents of non-covalent bond-mediated *ortho*-selective borylation

However, no matter in directing group assist *ortho*-borylation or in ligand-enabled *ortho*-borylation, all of them usually require already presence or installation of a directing group in substrates.

Use of common functional groups as directing groups would be more attractive alternatives, allowing for non-covalent bond interaction-controlled regioselective C-H borylation reaction. At present, non-covalent organocatalysis has been successfully applied into some reactions to achieve regioslective C-H borylation of aromatic substrates by employing hydrogen bonding, ion pairing, Lewis acid-base interaction and electrostatic interaction. In the followings, I will introduce some successful examples for regioselective C-H borylation of aromatic substrates controlled by using *non*-covalent bond interaction between substrates and iridium/bipyridine catalytic species.

The first *ortho*-selective C-H borylation of aromatic compounds controlled by non-covalent bond interaction was found by Smith *et al.* in 2012, in which hydrogen bonding interaction between the H atom of the Boc protected aniline substrate and the O atom of Bpin ligand favored *ortho*-selective C-H borylation[4] (**Scheme 2-4**).

In 2013, Kuninobu and Takai reported an *ortho*-selective C-H borylation of 2-phenylpyridine. In this reaction, 9-borabicyclo[3.3.1]nonane (9-BBN) was selected as a borylation reagent. The boryl group was introduced at the *ortho*-position of 2-phenylpyridine by Lewis acid-base interaction between the Lewis basic N atom and the Lewis acidic B atom.

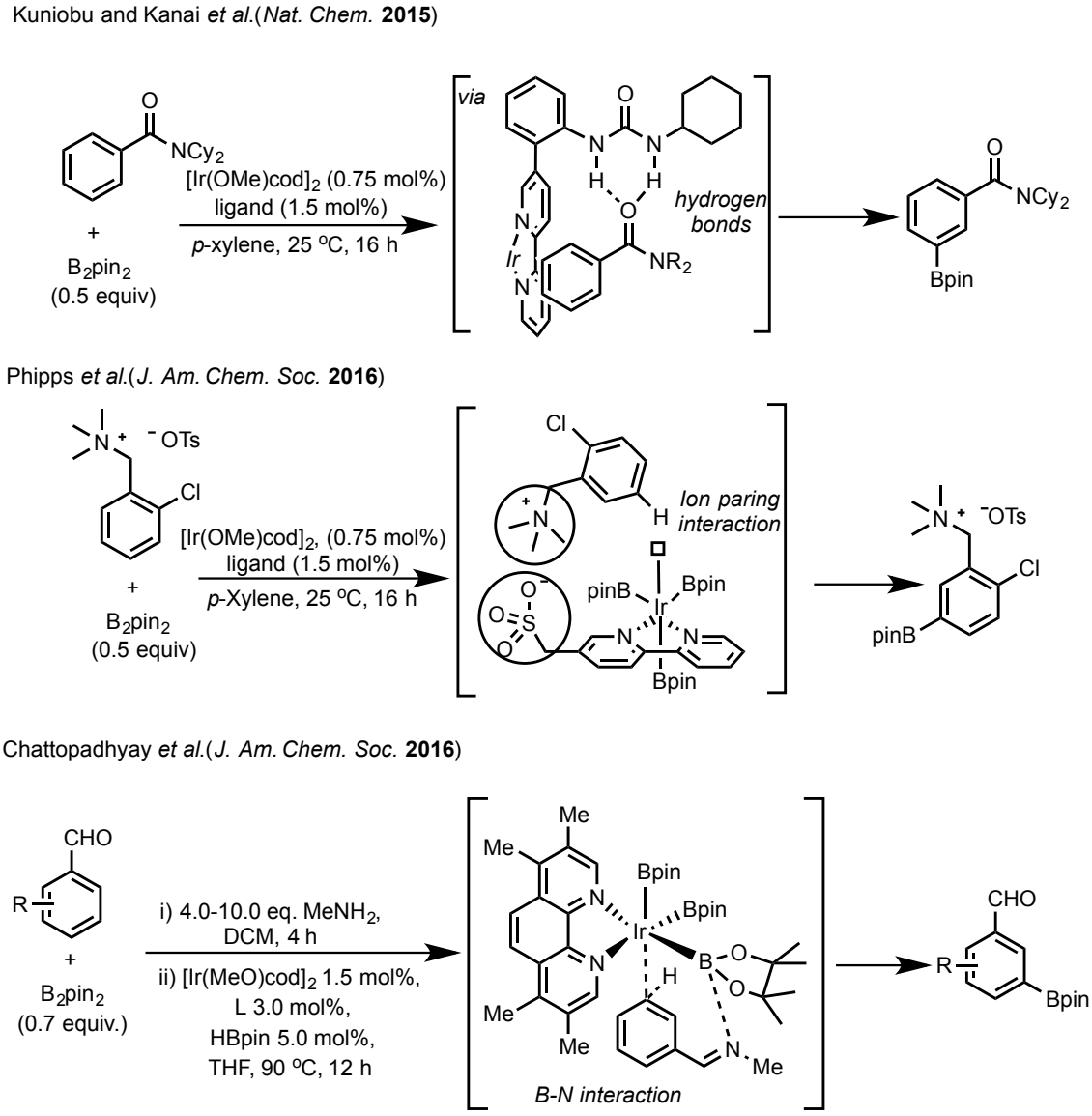


Scheme 2-4 Non-covalent bond interaction-controlled *ortho*-selective borylation

Moreover, *meta*- and *para*-selective C-H borylation of aromatic compounds have been achieved using non-covalent bond interaction in recent years. A significant breakthrough was made by our group in 2015. Our group developed an iridium-

catalyzed *meta*-selective C–H borylation of aromatic compounds using a newly designed ligand[5]. The hydrogen bonding interaction between the urea moiety of the designed ligand and a hydrogen-bond acceptor in a substrate places the iridium catalyst close to the *meta*-positon of amide substrates (**Scheme 2-5**).

In 2016, Phipps *et al*. also reported a *meta*-selective C-H borylation of aromatic compounds. In his work, the site selectivity was controlled by ion pairing interaction between substrate and designed ligand (**Scheme 2-5**).

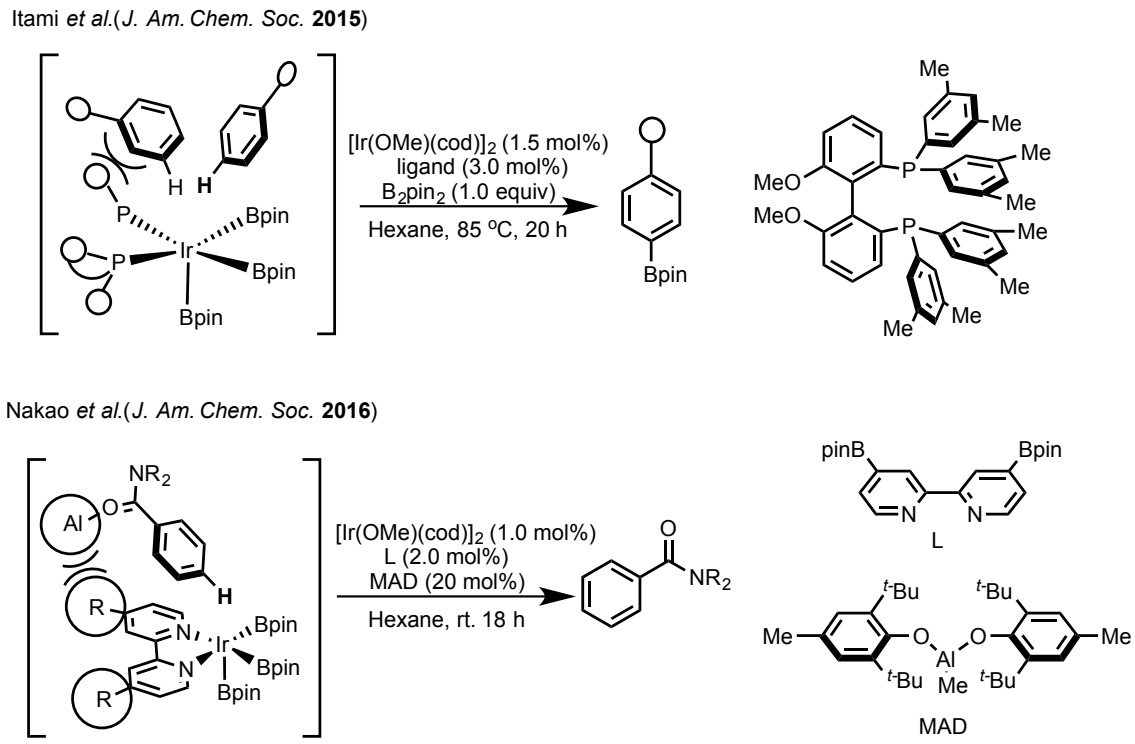


Scheme 2-5 Non-covalent interaction of B-N controlled *meta*-selective borylation

In the same year, Chattopadhyay reported a *meta*-selective C-H borylation of benzaldehydes. The reaction underwent through a non-covalent bond interaction between the boryl group of catalyst and the imine intermediates (**Scheme 2-5**).

As for *para*-selectivity[6], Itami and coworkers developed the first example of para-selective C-H borylation of aromatic compounds using an iridium catalyst bearing a bulky ligand in 2015. The para-selectivity increases with increasing bulkiness of the substituent on substrates (mon-substituted benzenes), indicating that the regioselectivity of this reaction is primarily controlled by steric repulsion between substrate and catalyst.

In 2016, Nakao and coworkers reported a method of *para*-selective C-H borylation of benzamides by using cooperative iridium/aluminum catalysis (**Scheme 2-6**). They thought that the regioselectivity is controlled by the steric repulsion between the substrates coordinating to the bulky aluminum catalysts and the iridium catalyst because the coordination shields the *ortho*- and *meta*- reactive position of substrates.



Scheme 2-6 Non-covalent interaction-controlled *para*-selective borylation

2.1.4 My research purpose

Before I started my research work, there was no method reported to achieve iridium catalyzed *ortho*-selective C-H borylation of aromatic compounds controlled by Lewis acid-base interaction between ligand and substrate. Our group is interested in the regiocontrol of C-H bond transformations using *non*-covalent bond interactions between catalysts and substrates.

Based on these methods and some experimental results, I found that the interaction of Lewis acid-base is a good way to promote *ortho*-selective C-H borylation of aromatic compounds, because it would be strong enough to overcome the steric repulsion between the iridium-boryl catalytic species and substituent(s) of the substrates. In the following sections, I will describe how to develop iridium catalyzed *ortho*-selective C-H borylation controlled by Lewis acid-base interaction during my doctor stage.

2.2 Development of Lewis Acid-Base Controlled *ortho*-Selective C-H Borylation of Aryl sulfides

2.2.1 Ligand design and synthesis

Inspired on the *meta*-selective C-H borylation of aromatic compounds developed by our group (**Figure 2.1-1**), I hypothesized that bipyridine type ligands with a Lewis acidic boryl group at *ortho*-position will be suitable for recognizing Lewis basic functional group of substrates and promoting *ortho*-selective C-H borylation[7]. As a result, identification of a ligand with suitable Lewis acidity and a substrate with suitable Lewis basicity is the key of this hypothesis (**Figure 2.1-2**).

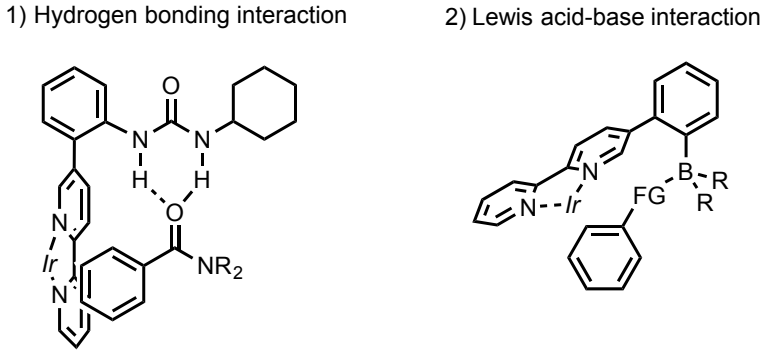
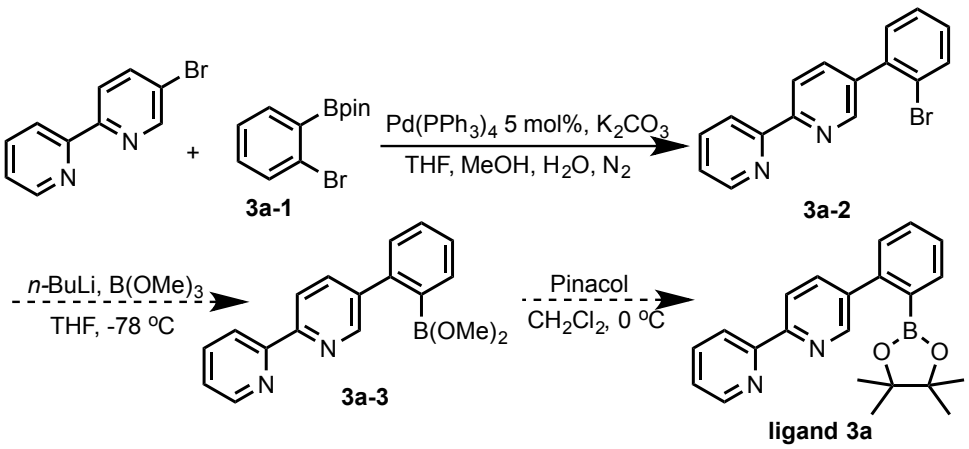


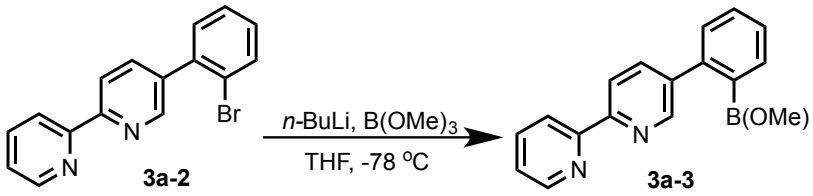
Figure 2.1 The hypothesis of *ortho*-selective C-H borylation reaction



Scheme 2-7 Planned synthetic route of **ligand 3a**

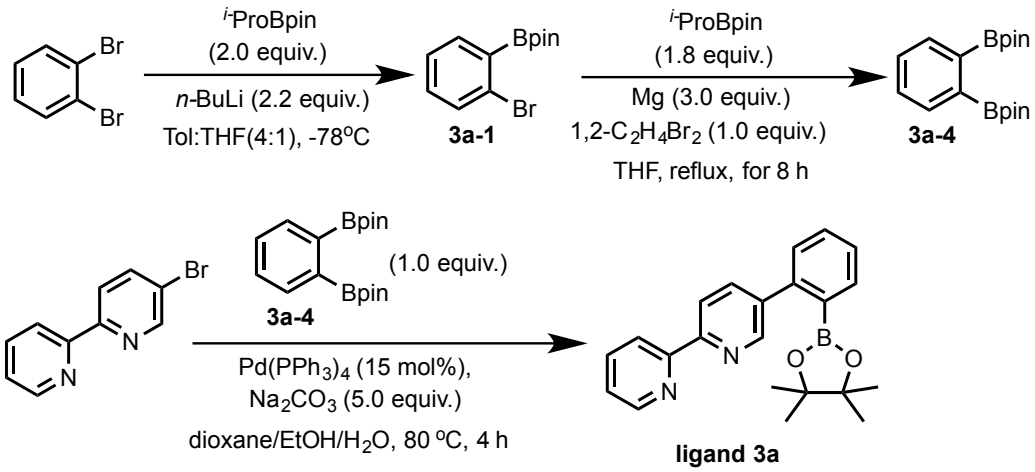
Hence, I initially began to design the synthetic route of target bipyridine type ligands. At first, I wanted to synthesize the target ligand with a Lewis acidic pinacolate boryl group at *ortho*-position according to the above synthetic route, because this kind of boryl group is comparatively stable than other boryl groups.

Table 2.1 The investigation of different bases for the reaction



entry	base	amount	yield(%)
1	*n*-BuLi	1.2 equiv.	20%
2	*sec*-BuLi	1.2 equiv.	10%
3	*t*-BuLi	1.2 equiv.	--
4	LiHMDS	1.2 equiv.	--

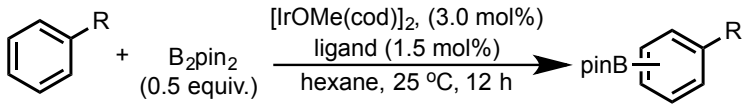
But there were some problems in this method. In the coupling reaction between 5-bromobipyridine and **3a-1**, self-coupling byproduct of **3a-1** was always obtained with intermediate **3a-2**, which decreased the efficiency of this synthetic method (**Scheme 2-7**). In addition, the reaction of introducing boryl reagent onto bipyridine ligand was often resulted in failure to give target compound (**Table 2.1**). One possibility for the failure is that the trimethylborate is very unstable and very sensitive to moisture and air.

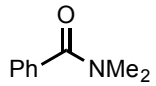
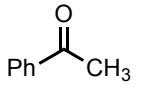
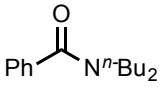
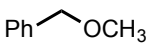
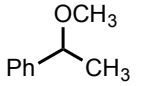
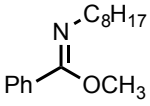
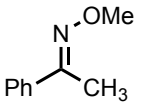
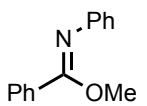


Scheme 2-8 The new synthetic route of **ligand-3a**

Therefore, I decided to change the synthetic route. Starting from 1,2-dibromobenzene, 1,2-diborylated intermediate **3a-4** was easily synthesized in good yield using organolithium and organomagnesium[8]. The coupling reaction between 5-bromobipyridine and intermediate **3a-4** catalyzed by $Pd(PPh_3)_4$ gave the target **ligand 3a** in 70% yield[9]. In addition, the coupling reaction also could avoid to produce self-coupling byproduct (**Scheme 2-8**).

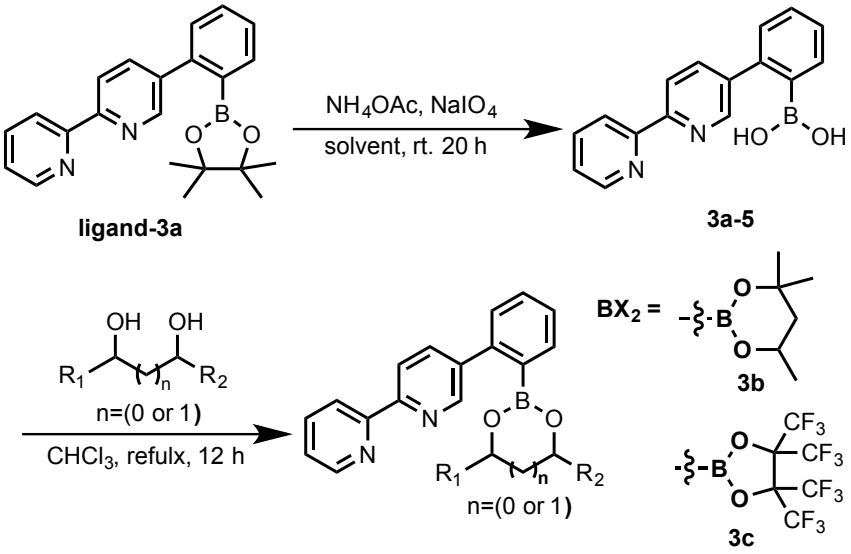
Table 2.2 The investigation of different Lewis base substrates



substrates	ligand	yield(%) (*mono*)	ratio of *meta* to *para*	yield(%) (*di*)
	dtbpy	2.0 %	0.6	--
	Ligand 3a	2.0 %	0.8	--
	dtbpy	36.0 %	1.1	10.0 %
	Ligand 3a	35.2 %	1.2	7.0 %
	dtbpy	5.4 %	0.3	--
	Ligand 3a	--	--	--
	dtbpy	--	--	--
	Ligand 3a	--	--	--
	dtbpy	5.4%	0.2	--
	Ligand 3a	0.9%	0.2	--
	dtbpy	28.4 %	0.9	--
	Ligand 3a	23.7 %	1.4	--
	dtbpy	42.6 %	0.8	10.0 %
	Ligand 3a	32.1 %	0.8	7.0 %
	dtbpy	15.2 %	1.1	--
	Ligand 3a	10.5 %	0.7	--

With **ligand 3a** in hand, I started to investigate a series of aromatic compounds, all of which contain a Lewis basic center such as carbonyl, ether and imine. The dtbpy (4,4'-dimethyl-2,2'-dipyridyl) was used as a control ligand. Unfortunately, I did not observe *ortho*-borylated product from these substrates. In many cases, the C-H borylation

reaction did not proceed. There were some entries giving a mixture of *meta*- and *para*-borylated products in low yield. I thought that these unsatisfactory results were probably caused by low reaction temperature. But when I carried out some reactions at 80 ^{o}C, the yield of C-H borylation reaction did not increase. Regarding to the low yield of C-H borylation for these substrates, selecting a suitable solvent is necessary for improving it[10]. On the other hand, how to improve the ratio of *ortho*-borylated product in the reaction is more important. By analyzed this C-H borylation reaction, I envisioned that there are three main factors for controlling *ortho*-regioselectivity, including Lewis acidity of bipyridine type ligand, steric hindrance between ligand and substrate, and Lewis basicity of substrates. **Ligand 3a** with a pinacolate boryl group as Lewis acid center, the four methyl groups are too sterically hindered for the approaching of ligand and substrate. Besides, these methyl groups have electron donating effects to the boron atom, which is also unfavorable for Lewis acid-base interaction.



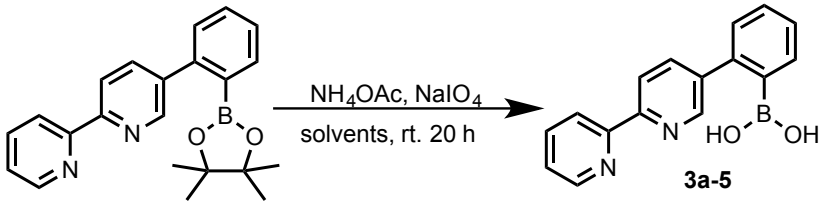
Scheme 2-9 The strategy for the synthesis of new ligands

Keeping these reasons in mind, I would like to synthesize some ligands with less steric hindrance and stronger Lewis acidity. My strategy is that employing **ligand 3a** as starting material, the pinacol moiety can be removed by hydrolysis reaction to generate boric acid intermediate **3a-5**[11], then some other diols with different substituents (especially for EWG to increase Lewis acidity of boron atom) would be introduced to

the boron atom (**Scheme 2-9**)[12-13].

As for the hydrolysis reaction, I screened several conditions as shown in **Table 2.3**. The hydrolysis reaction could not give good yield of **3a-5** in organic solvents because the oxidant $NaIO_4$ is difficult to dissolve in these solvents. However, the hydrolysis product could be obtained in 40% using acetone as solvent. Encouraged by this result, I tried to use a mixture solvent of acetone/H_2O to increase the solubility of $NaIO_4$. Finally, a good condition was developed successfully, which provided a convenient way to synthesize some new ligands.

Table 2.3 Optimization process for hydrolysis reaction



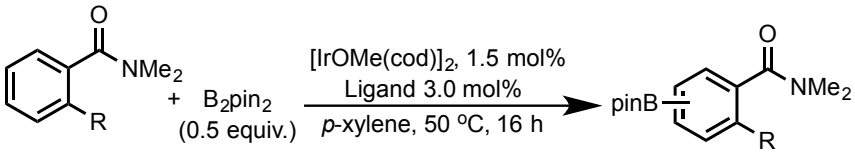
entry	sovlent	yield(%)
1	MeOH	20%
2	MeCN	5%
3	acetone	40%
4	THF	--
5	acetone/H_2O (20 : 1)	48%
6	acetone/H_2O (10 : 1)	63%
7	acetone/H_2O (1 : 1)	80%

According to my strategy, new ligands were successfully synthesized. In order to reduce the steric hindrance between ligand and substrate, **ligand-3b** was synthesized by introducing 2-methylpentane-2,4-diol to the boron atom. **Ligand-3c** with 2,3-bis(trifluoromethyl)butane-2,3-diol was aimed at enhancing Lewis acidity.

I also tried to optimize the condition of C-H borylation reaction. After studying a series of solvents and temperature, I found that aromatic substrates with B_2pin_2 (0.5 equiv.) in *p*-xylene under 55 ^oC could give rise to good yields of borylated product. Under the best conditions, I continued to investigate substrates using **ligand-3b** and **ligand-3c**. The *ortho*-substituted benzamides was selected as substrates based on our

previous results and the screening results were shown in **Table 2.4**. Compared with **ligand-3a**, the yield of borylated product was dramatically improved using **ligand-3b** in the case of *ortho*-substituted substrates, but the *ortho*-borylated isomer was still not formed in these cases. The low Lewis acidity of **ligand-3b** could account for this undesirable result. As regards to **ligand-3c**, most entries were failure to give borylated products. Poor solubility of it in *p*-xylene was one of reasons for the failure results. Therefore, a ligand with enough strong Lewis acidity, good solubility and less steric hindrance was very essential for *ortho*-selectivity.

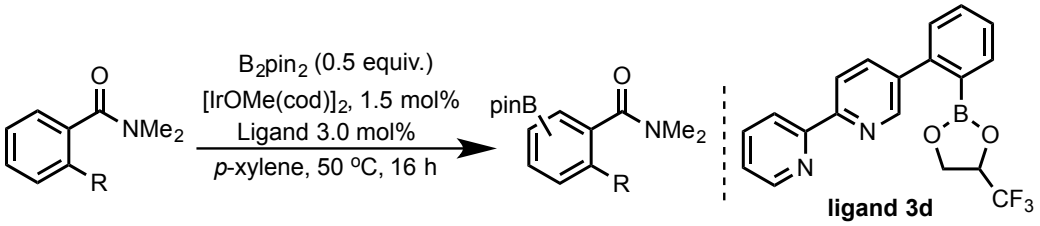
Table 2.4 The screening results of **ligand 3b** and **ligand 3c**



R	ligand	yield(%)	ratio of *meta* to *para*
-Me	dtbpy	60.3 %	1.0
	Ligand 3b	54.5 %	1.5
-OMe	dtbpy	59.0 %	1.3
	Ligand 3b	41.7 %	1.8
$-CF_3$	dtbpy	40.1 %	0.9
	Ligand 3b	22.8 %	1.4
-COOMe	dtbpy	35.6 %	2.1
	Ligand 3b	47.4 %	2.5
-Me	dtbpy	48.2 %	0.7
	Ligand 3c	5.0 %	1.0
-OMe	dtbpy	63.7 %	0.9
	Ligand 3c	--	--
$-CF_3$	dtbpy	30.6 %	1.1
	Ligand 3c	--	--
-COOMe	dtbpy	56.4 %	0.8
	Ligand 3c	--	--

Ligand-3d bearing one trifluoromethyl group in the 1,3,2-dioxaborolanyl group was synthesized in this context. The screening results were shown in **Table 2.5**. By using dtbpy as ligand, the C-H borylation of substrates with electron donating group gave a ratio of *meta*- and *para*-isomer about 1 : 1, which was lower than those of substrates containing electron withdrawing group. This result is consistent with the rule of electronic effect on C-H borylation, in which reactions of electron-poor C-H bond was shown to be faster than those of electron-rich C-H bond[14]. In the case of 2-methoxy-*N*,*N*-dimethylbenzamide, I observed an interesting result the borylation reaction gave a ratio of *meta*- and *para*-isomer in 1 : 2.

Table 2.5 The screening results of **ligand 3d**



R	ligand	yield(%)	ratio of *meta* to *para*
-Me	dtbpy	55.3 %	1 : 1
	Ligand 3d	33.6 %	2 : 1
-OMe	dtbpy	60.8 %	1 : 1
	Ligand 3d	**52.7 %**	**1 : 2**
-CF_3	dtbpy	59.5 %	3 : 1
	Ligand 3d	23.0 %	2 : 1
-COOMe	dtbpy	47.2 %	2 : 1
	Ligand 3d	40.4 %	2 : 1

One possibility to account for this interesting result (*para*-position of the amide functionality is *meta*-position to methoxy functionality) is that there's a very weak interaction between methoxyl group and **ligand-3d**. However, this interaction is not strong enough to promote *ortho*-selectivity. From this point of view, the type of anisole compounds will be suitable for ligand-substrate interaction. Then, I investigated this type of substrates and the results were shown in **Table 2.6**.

To my delight, the C-H borylation reaction of thiolanisole catalyzed by **ligand-3d** could proceed with high *ortho*-selectivity in 57% yield. Whereas, the C-H borylation reaction gave a mixture of *meta*- and *para*-borylated products in the case of anisole and *N,N*-dimethylamine. The sterically hindered substituents of *N,N*-dimethylamine make the C-H borylation difficult to proceed at *ortho*-position.

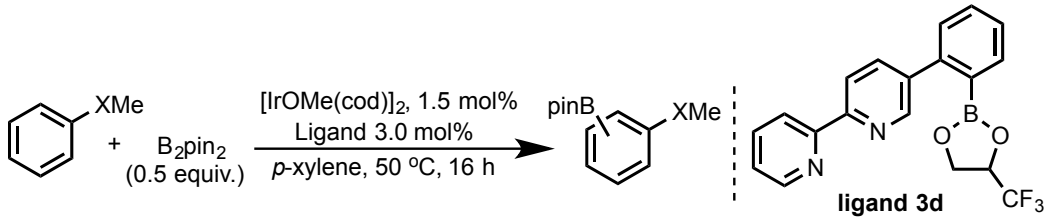
The enthalpy change for a Lewis acid-base reaction can be predicted using the Drago-Wayland equation[15] (DH (in kJ/mol) = -4.184 ($C_AC_B + E_AE_B$)). I calculated the DH values using model compounds, such as diethyl sulfide (instead of thiolanisole), diethyl ether (instead of anisole), and BF_3 (instead of **ligand-3d**);

Et_2S-BF_3: DH (in kJ/mol) = -4.184 (1.62 x 7.4 + 9.88 x 0.339) = -64.2

Et_2O-BF_3: DH (in kJ/mol) = -4.184 (1.62 x 3.25 + 9.88 x 0.936) = -60.7

The energy of the S-B interaction is lower than O-B interaction which indicates that the S-B interaction is stronger than O-B interaction. These results provide a good explanation for the reason why the C-H borylation reaction only gave a mixture of *meta*- and *para*-borylated product in the case of anisole.

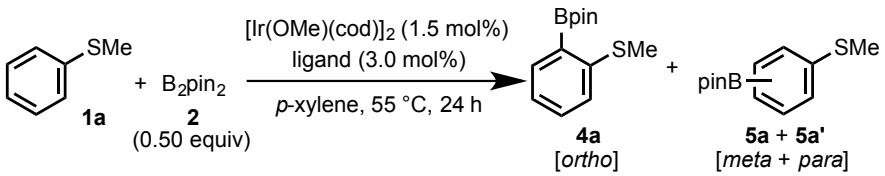
Table 2.6 The screening results of **ligand 3d**



substrates	ligand	yield(%)	ratio of (*o* : *m*+*p*)	ratio of (*m* : *p*)
PhOMe	dtbpy	85.0 %	--	2.5
	Ligand 3d	66.2 %	--	3.8
PhSMe	dtbpy	51.0 %	0.2	--
	Ligand 3d	**57.5 %**	**>30**	**--**
$PhNMe_2$	dtbpy	50.0 %	--	1.3
	Ligand 3d	34.7 %	--	1.8
$PhPMe_2$	dtbpy	--	--	--
	Ligand 3d	--	--	--

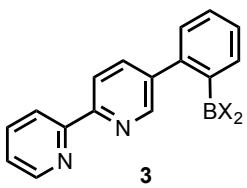
2.2.2 Ligand effects on *ortho*-selective C-H borylation of aryl sulfides

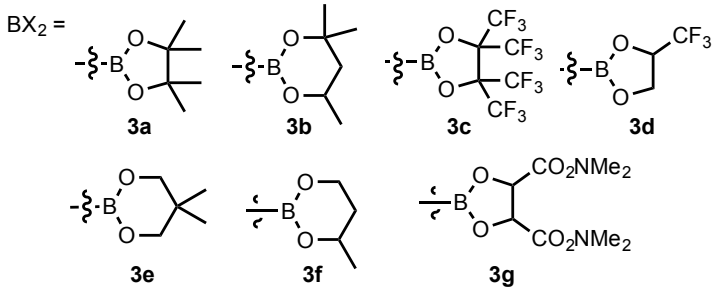
After getting this good result, I turned my attention to study ligand effects on *ortho*-selective C-H borylation of thiolanisole derivatives. Therefore, several bipyridine-type ligands with a boryl group were investigated (**Scheme 2-10**). In the case of **ligand-3a** with a pinacolboryl group, the [*ortho*/(*meta* + *para*)] ratio was about 3.8. I thought that the reason for this result is the same as previous screening result. The pinacolboryl group was too bulky for the ligand-substrate interaction. Then, I investigated several ligands with a less sterically hindered boryl group. The ratio of the products, however, was not increased further using **ligands 3b**, **3e**, or **3f**. I considered that the moderate ratios must be due to the low Lewis acidity of ligands compared with **ligand-3d**. In addition, the desired reaction did not proceed using **ligand-3c** bearing four trifluoromethyl groups in the 1,3,2-dioxaborolanyl group. Besides its poor solubility, the excessively strong interaction between ligand and a sulfur atom is another reason.



entry	ligand	yield / %	ratio of **4a**/**5a+5a'**
1	dtbpy	70	0.22
2	**3a**	31	3.8
3	**3b**	51	3.2
4	**3c**	<1	—
5	**3d**	64	>30
6	**3e**	55	2.3
7	**3f**	64	2.8
8	**3g**	<1	—

dtbpy = 4,4'-dimethyl-2,2'-dipyridyl.



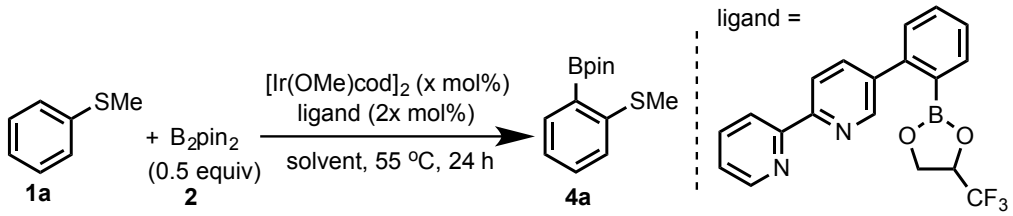


Scheme 2-10 The ligand effect on C-H borylation reaction of thioanisole

2.2.3 The effect of solvent and catalyst loading

In order to improve the yield of borylation reaction, I investigated several catalyst amounts and solvents. I found 3.0 mol% of the catalyst was the best, and gave the borylated product in 75% yield[16] and the ratio of [*ortho*/(*meta* + *para*)] was over 30. By increasing the loading of the catalyst, the yield and ratio decreased, probably due to the too concentrated reaction mixture. Then, I investigated several solvents. As a result, *p*-xylene was the best compared with other solvents, because *p*-xylene is non-polar solvent, which is favorable for the interaction of Lewis acid-base. In addition, *p*-xylene also has good solubility for substrates and ligands. The yield of the C-H borylation reaction could reach up to 75% and the ratio was more than 30:1 (**Table 2.7**).

Table 2.7 The screening results of catalyst loading and solvents



p-xylene

x (mol%)	yield / %	ratio[a]
1.5	47	>30
3.0	75	>30
5.0	63	10
8.0	42	4

[a] *ortho* / *meta* + *para*.

$[Ir(OMe)cod]_2$ (3.0 mol%)

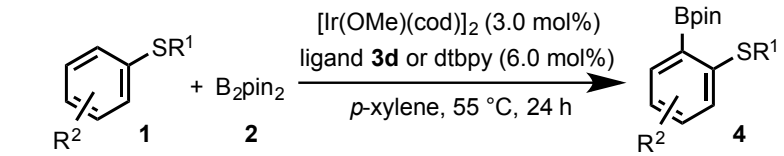
solvent	yield / %	ratio[a]
hexane	8	>30
p-xylene	75	>30
THF	19	>30
dioxane	35	5.5
EtOAc	31	7.5
methyl *tert*-butyl ether	--	--
DME	--	--
Et_2O	--	--
$CHCl_3$	--	--

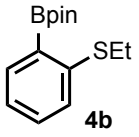
[a] *ortho* / *meta* + *para*.

2.2.4 Substrates scope for *ortho*-selective C-H borylation of aryl sulfides

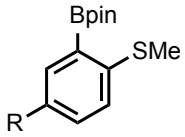
The substrate scope was then studied under the optimized conditions (**Table 2.7**). In general, treatment of thioanisole (**1a**) with bis(pinacolato)diboron (**2**) in the presence of an iridium catalyst $[Ir(OMe)(cod)]_2$ and **ligand 3d** at 55 °C gave borylated product with high *ortho*-regioselectivity. The C-H borylation proceeded with high *ortho*-selectivity using ethyl(phenyl)sulfane (**1b**)[17]. *ortho*-Borylated products **4c**-**4f** were obtained without inhibition by the functional groups and/or loss of the functional groups at the *para*-positions. In the case of (4-methoxyphenyl)(methyl)sulfane (**1c**), the C-H borylation occurred at the *ortho*-position of the methylthio group, not of the methoxy group. In the case of 4-phenylthioanisole **1g**, *ortho*-selective C-H borylated product **4g** was obtained using ligand **3d**, whereas C-H borylation occurred at the other aromatic ring at the 4-position (**5g** and **5g′**) using the dtbpy ligand. In the case of *meta*-substituted thioanisole derivatives **1h**-**1u**, the C-H borylation regioselectively proceeded at the *ortho*-position with less steric hindrance between the two possible *ortho*-reaction sites using ligand **3d**. These results were in sharp contrast to those of reactions using the dtbpy ligand, in which C-H borylation occurred predominantly at the *meta*-positions of thioanisoles. The functional groups of thioanisoles **1h**-**1u** remained unchanged during the reactions. More interestingly, the reaction proceeded only at the *ortho*-position of a sulfur atom whereas ester, amide, cyano, pyrrolidinyl, and morpholinyl groups in **4p**, **4q**, **4s**, **4t**, and **4u** could work as Lewis basic sites and coordinate to the boryl group of the ligand. The desired reaction did not proceed when using 3-(methylthio)pyridine, 3-(methylthio)furan, and 3-(methylthio)-1-(trimethylsilyl)-1*H*-pyrrole. In the case of 3-(methylthio)thiophene, a mixture of 5-borylated and 2,5-diborylated products was obtained, but the ratio of regioisomers was almost the same in both ligand **3d** and dtbpy. The yields of the borylated products using ligand **3d** were higher than those using the dtbpy ligand in several substrates, such as **4d**-**4f**, **4h**, and **4k**. These results suggest that ligand **3d** accelerates the C-H borylation reaction by capturing the substrates using a Lewis acid-base interaction.

Table 2.7 The results of *ortho*-selective C-H borylation of different aryl sulfides





4b
72% [>30]^{b}
83% [0.29]^{c}

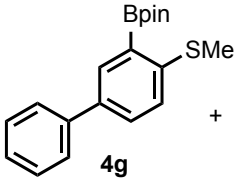


4c R= OMe
66% [>20]^{b}
63% [1.0]^{c}

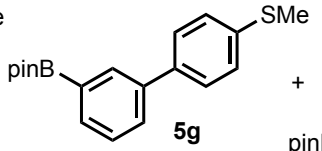
4d R= Me
73% [>30]^{b}
61% [2.0]^{c}

4e R= Cl
80% [12]^{b}
71% [2.0]^{c}

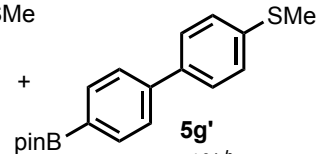
4f R= Br
85% [6.6]^{b}
76% [3.0]^{c}



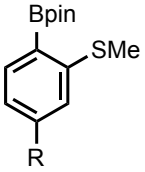
4g
86%^{b}
<1%^{c}



5g
<1%^{b}
54%^{c}



5g'
<1%^{b}
29%^{c}



4h R= NMe_2
76% [>30]^{b}
63% [<0.01]^{c}

4i R= OMe
60% [>30]^{b}
69% [<0.01]^{c}

4j R= Me
64% [>30]^{b}
62% [0.16]^{c}

4k R= Et
88% [>30]^{b}
74% [<0.01]^{c}

4l R= ^{i}Pr
62% [>30]^{b}
63% [<0.01]^{c}

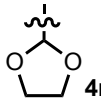
4m R= $SiMe_3$
83% [>30]^{b}
78% [<0.01]^{c}

4n R= Cl
64% [5.1]^{b}
75% [<0.01]^{c}

4o R= Br
79% [6.7]^{b}
72% [0.13]^{c}

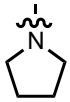
4p R= CO_2Me
89% [>30]^{b}
83% [<0.01]^{c}

4q R= $CONMe_2$
77% [>30]^{b}
85% [<0.01]^{c}

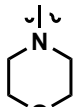


4r
90% [>30]^{b}
92% [<0.01]^{c}

4s R= CN
75% [>30]^{b}
82% [<0.01]^{c}



4t
70% [>30]^{b}
63% [<0.01]^{c}



4u
73% [>30]^{b}
75% [<0.01]^{c}

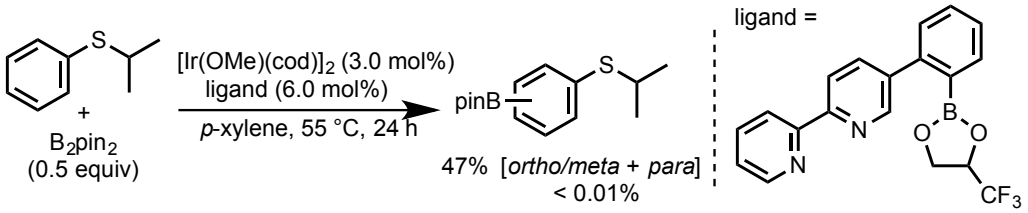
[a] **2a** (0.50 equiv). The yield is a total yield of *ortho*-, *meta*-, and *para*-products.
[b] Ligand **3d** case: [*ortho*/*meta* + *para*] ratios. [c] dtbpy case: [*ortho*/*meta* + *para*] ratios

2.2.5 Control experiments

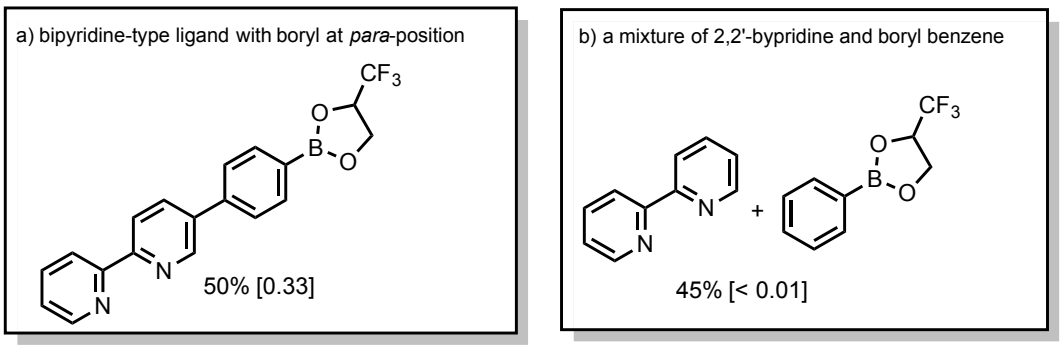
In order to confirm the existence of a Lewis acid-base interaction between ligand and substrates, I performed some control experiments and revealed the following: (1) the *ortho*-selectivity highly depended on the Lewis acidity of the boryl groups, as shown in **Scheme 2-11**; (2) the [*ortho*/(*meta* + *para*)] ratio in non-polar solvents was much higher than that in polar solvents, such as dioxane and ethyl acetate (**Table 2.7**); (3) the *ortho*-selectivity decreased in the case of aryl sulfides with a bulky substituent on the sulfur atom, such as isopropylthiobenzene ([*ortho*/(*meta* + *para*)] ratio <0.01 (47% yield)); and (4) the *ortho*-selectivity was not observed in several reactions using the following control ligands: (a) bipyridyl-type ligand **3h** with a boryl group at the *para*-position of the phenyl group instead of at the *ortho*-position; and (b) a mixture of 2,2'-bipyridine and borylbenzene **3i** without covalently connecting the two components. These results indicate that the Lewis acid-base interaction worked during the reaction and played an important role in the high *ortho*-selectivity.

Figure 2.2 Some experimental results supporting Lewis acid-base interaction

(3) Steric effect on *ortho*-selective C-H borylation of aryl sulfides



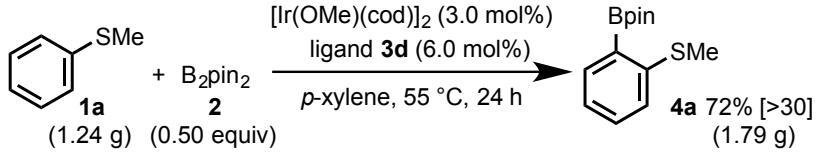
(4) Ligand effect on *ortho*-selective C-H borylation of aryl sulfides



[a] The yield is a total yield of *ortho*-, *meta*-, and *para*-products. [b] [*ortho*/*meta* + *para*] ratios are shown in the square brackets

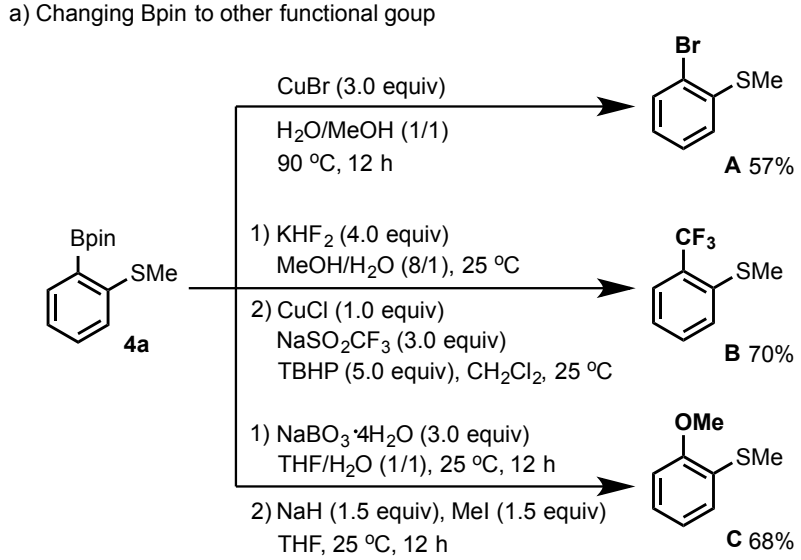
2.2.6 Application of *ortho*-selective C-H borylation

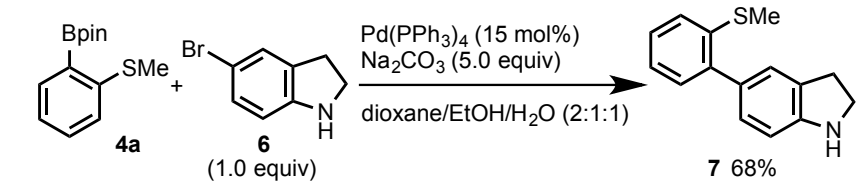
After finishing the main work of this research, I devoted to exploring the application reaction of this method. I found that this borylation reaction could proceed in good yield with high *ortho*-selectivity, even in gram-scale (**Scheme 2-11**). Treatment of 1.24 g of thioanisole (**1a**) with diboron **2** in the presence of iridium/**3d** catalyst gave 1.79 g of *ortho*-borylated product **4a** in 72% yield ([*ortho*/*meta* + *para*] >30).



Scheme 2-11 Gram-scale of *ortho*-selective C-H borylation of aryl suldfide

As we all know, boryl group could be converted to other various functional groups. Thus, I performed some reaction changing boryl group to other functional groups such as

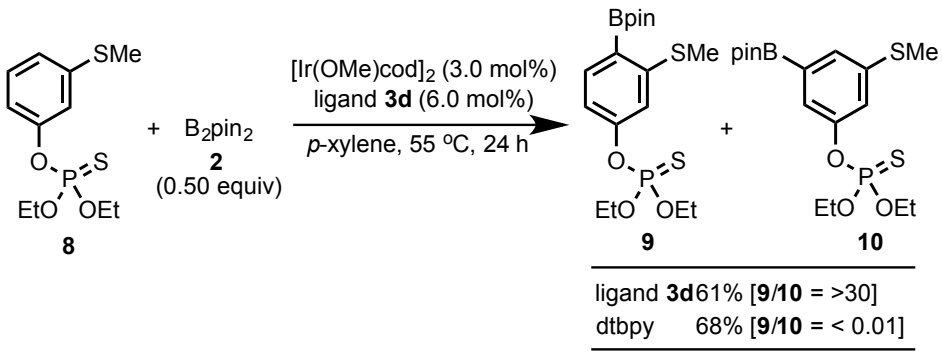




Scheme 2-12 Applications of *ortho*-borylated thioanisole **4a**

a bromine atom[18], a trifluoromethyl group[19], and a methoxy group[20], which demonstrates the synthetic utility of the borylated products. In addition, 2-borylated aryl sulfides can be used as substrates to synthesize intermediate of factor Xa inhibitors by the Suzuki-Miyaura cross-coupling reaction[21]. Palladium-catalyzed Suzuki-Miyaura cross-coupling between *ortho*-borylated thioanisole **4a** and 5-bromoindoline (**6**) gave the desired product in 68% yield without protecting the NH group (**Scheme 2-12**).

The *ortho*-selective C-H borylation was also applied to bioactive compound **8**, which is an insecticide (**Scheme 2-13**)[22]. Treatment of **8** with bis(pinacolato)diboron (**2**) in the presence of an iridium catalyst $[Ir(OMe)(cod)]_2$ and ligand **3d** gave *ortho*-borylated product **9** in 61% yield (**9**/**10** >30). This result, too, was in sharp contrast to that of the reaction using dtbpy, in which borylation proceeded mainly at the *meta*-position of **8** (**9**/**10** = <0.01). Interestingly, the reaction occurred exclusively at the *ortho*-position of the sulfide group, even though there are two sulfur-containing functional groups (i.e., sulfide and thiophosphate groups) in **8**.



Scheme 2-13 *ortho*-Selective C-H borylation of insecticide **8**

2.3 Summary

In summary, I successfully developed an iridium/bipyridine-catalyzed *ortho*-selective C-H borylation of aromatic sulfides. The regioselectivity was controlled by a Lewis acid-base interaction between a boryl group of bipyridine ligand **3d** and a sulfur atom of aryl sulfides. The present reaction is the first example of regioselective C-H transformations controlled by a Lewis acid-base interaction between a ligand and substrate. The Lewis acid-base interaction is strong enough to overcome the steric repulsion between the catalytically active iridium-boryl species and a substituent of the substrates. The C-H borylation proceeded with high *ortho*-selectivity and functional group tolerance, even in gram-scale. In addition, the reaction could be applied to late-stage *ortho*-selective C-H borylation of a bioactive molecule. A bioactive molecule was synthesized from an *ortho*-borylated product. Because many C-H transformations require harsh reaction conditions, the regiocontrol mediated by the strong but reversible Lewis acid-base interaction will become a powerful general method.

References

1. For reviews, see: a) Ishiyama, T.; Isou, H.; Kikuchi, T.; Miyaura, N. *Chem. Commun.* **2010**, *46*, 159; b) Robbins, D. W.; Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 4068; c) Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2012**, *134*, 134; d) Ros, A.; Lopez-Rodriguez, R.; Estepa, B.; Alvarez, E.; Fernandez, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 4573; e) Xiao, B.; Li, Y.-M.; Liu, Z.-J.; Yang, H.-Y.; Fu, Y. *Chem. Commun.* **2012**, *48*, 4854.
2. For directing group assist *ortho*-selective C-H borylation, see: a) Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 7534; b) Kawamorita, S.; Ohmiya, H.; Hara, K.; Fukuoka, A.; Sawamura, M. *J. Am. Chem. Soc.* **2009**, *131*, 5058; c) Kawamorita, S.; Miyazaki, T.; Ohmiya, H.; Iwai, T.; Sawamura, M. *J. Am. Chem. Soc.* **2009**, *131*, 5058.
3. For ligand enabled *ortho*-selective C-H borylation, see: a) Ghaffari, B.; Preshlock, S. M.; Plattner, D. L.; Staples, R. J.; Maligres, P. E.; Krska, S. W.; Maleczka, R. E. and Smith III, M. R. *J. Am. Chem. Soc.* **2014**, *136*, 14345; b) Bisht R. and Chattopadhyay, B. *J. Am. Chem. Soc.* **2016**, *138*, 84; c) Wang, G.; Liu, L.; Wang, H.; Ding, Y. S.; Zhou, J.; Mao, S.; and Li, P. F. *J. Am. Chem. Soc.* **2017**, *139*, 91.
4. For non-covalent bond interaction controlled *ortho*-selectivity, see: a) Roosen, P. C.; Kallepalli, V. A.; Chattopadhyay, B.; Singleton, D. A.; Maleczka, R. E. and Smith III M. R. *J. Am. Chem. Soc.* **2012**, *134*, 11350; b) Kuninobu, Y.; Iwanaga, T.; Omura, T.; Takai, K. *Angew. Chem. Int. Ed.* **2013**, *52*, 4431.
5. For non-covalent bond interaction controlled *meta*-selectivity, see: a) Kuninobu, Y.; Ida, H.; Nishi, M.; Kanai, M. *Nature Chem.* **2015**, *7*, 712; b) Davis, H. J.; Mihai, M. T.; Phipps, R. J. *J. Am. Chem. Soc.* **2016**, *138*, 12759; c) Bisht R. and Chattopadhyay, B. *J. Am. Chem. Soc.* **2016**, *138*, 84.
6. For non-covalent bond interaction controlled *para*-selectivity, see: a) Saito, Y.; Segawa, Y.; Itami, K. *J. Am. Chem. Soc.* **2015**, *137*, 5193; b) Yang, L. C.; Semba, K.; Nakao, Y. *Angew. Chem. Int. Ed.* **2017**, 56, 4853.
7. For a review on supramolecular catalysis, see: Raynal, M.; Ballester, P.; Vidal-Ferran, A.; Leeuwen, P. W. N. M. *Chem. Soc. Rev.* **2014**, *43*, 1660.
8. Seven, Ö.; Bolte, M.; Lerner, H.-W.; Wagner, M. *Organometallics* **2014**, *33*, 1291.
9. Mahata, K.; Frischmann, P. D.; Würthner, F. *J. Am. Chem. Soc.* **2013**, *135*, 15656.

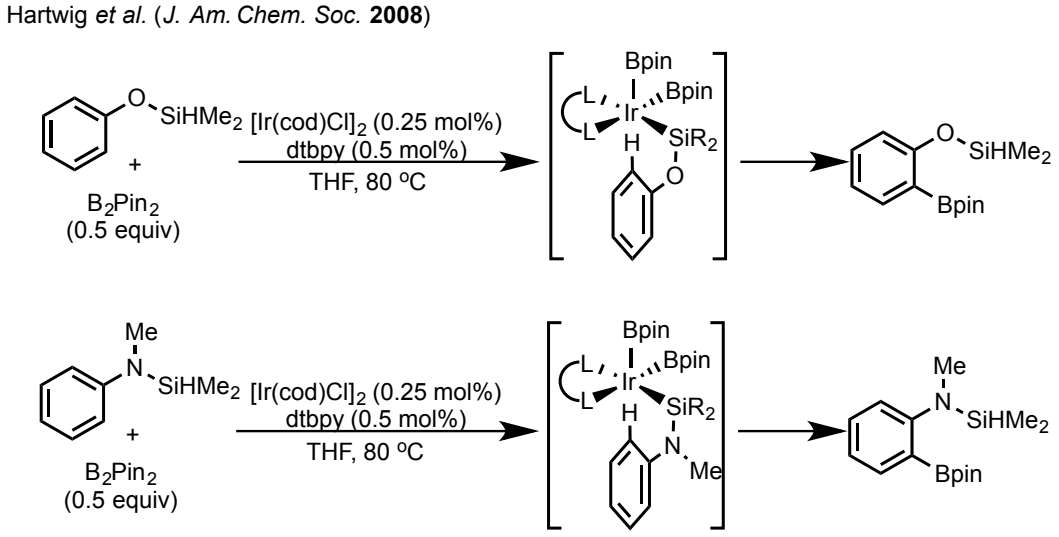
10. For a review on mild metal-catalyzed C-H transformations, see: Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900.
11. Wood, J. L. L.; Marciasini, D.; Vaultier, M.; Pucheault, M. *Synlett* **2014**, *25*, 551.
12. Tsoi, Y.-T.; Zhou, Z.; Yu, W.-Y. *Org. Lett.* **2011**, *13*, 5370.
13. Kaupp, G.; Naimi-Jamal, M. R.; Stepanenko, V. *Chem. Eur. J.* **2003**, *9*, 4156.
14. Boller, T. M.; Murphy, J. M.; Hapke, M.; Ishiyama, T.; Miyaura, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 14263.
15. R. S. Drago, *Coord. Chem. Rev.* **1980**, *33*, 251.
16. When an excess amount of B_2pin_2 (1.0 equiv) was treated with **1a**, a mixture of mono- (**4a**) and di-borylated products was formed quantitatively (mono:di = 55:45).
17. In the case of a benzyl thioether (benzylphenylsulfane), *ortho*-C-H borylation occurred at the aromatic ring of the benzyl group (not at the phenyl group) and the corresponding borylated product was obtained in 73% yield.
18. Thompson, A. L. S.; Akula, M. R.; Huffman, J. W. *Synthesis* **2005**, 547.
19. Dubbaka, S. R.; Salla, M.; Bolisetti, R.; Nizalapur, S. *RCS Adv.* **2014**, *4*, 6496.
20. Lv, F. P.; Li, Z. F.; Hu, W. H.; Wu, X. H. *Bioorg. Med. Chem.* **2015**, *23*, 7661.
21. a) Uetake, Y.; Niwa, T.; Hosoya, T.; *Org. Lett.* **2016**, *18*, 2758; b) Varnes, J. G.; Wacker, D. A.; Jacobson, I. C.; Quan, M. L.; Ellis, C. D.; Rossi, K. A.; He, M. Y.; Luettgen, J. M.; Knabb, R. M.; Bai, S.; He, K.; Lam, P. Y. S.; Wexler, R. R. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 6481.
22. Wuppertal-Elberfeld, E. S.; Schrader, G. Thiophosphoric Acid Esters. Ger. Offen. DE 1101406, March 22, 1956.

Chapter 3

Development of Iridium/Bipyridine-Catalyzed *ortho*-Selective C-H Boylation of Phenol and Aniline Derivatives

3.1 Introduction

Phenol and aniline derivatives are very useful compounds in organic chemistry. For example, phenols are widely found in numerous natural products, bioactive compounds, pharmaceuticals, and polymers[1]. Anilines as raw materials have been widely used in different fields over the past hundred years, such as dyes and pigments, agricultural chemicals and pharmaceuticals[2]. In addition, phenols and anilines also constitute common versatile building blocks in organic synthesis. Therefore, the development of methods for site-selective C-H functionalization of phenol and aniline derivatives is of great importance.



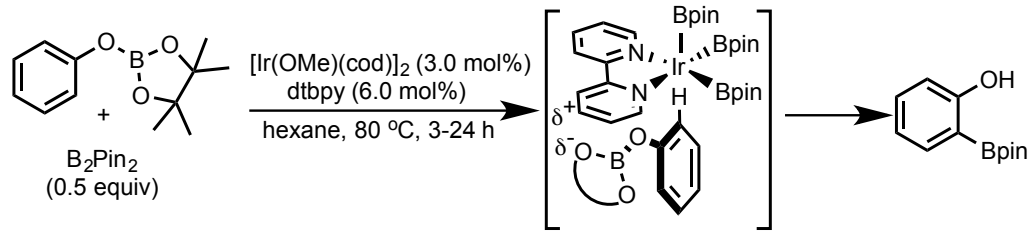
Scheme 3-1 Directing group-assisted *ortho* C-H borylation of phenols and anilines

ortho-C-H borylation of phenol and aniline derivatives has been accomplished by catalyst or substrate modifications in the past few years. Generally, these methods can

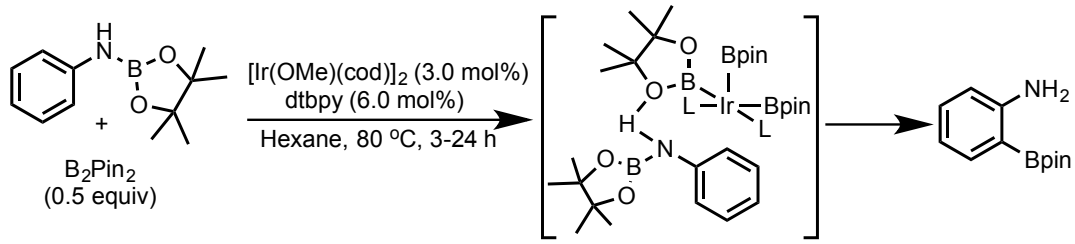
be divided into the following two strategies. One is the directing group-assisted *ortho* C-H borylation of phenol and aniline substrates. In 2008, Hartwig reported an example, in which the use of an alkyl hydrosilyl functionality as directing group controlled the borylation at the *ortho* position of a hydroxyl or amino substituent[3]. The directing group could coordinate with iridium center and bring the iridium boryl catalytic species close to *ortho* position that will facilitate the cleavage of *ortho* C-H bond (**Scheme 3-1**).

Besides, Smith also developed two methods of *ortho* C-H borylation of phenol and aniline substrates. By using non-covalent bond interaction between iridium boryl catalytic species and substrates, they could achieve *ortho* C-H borylation of Bpin protecting phenols and anilines (**Scheme 3-2**). In the first example of using Bpin protecting phenols as substrates, an electrostatic interaction between the oxygen atom of the boryl moiety of the substrates and the bipyridine ligand of the catalyst is the key activating and controlling element for *ortho* C-H borylation. In the case of aniline derivatives, hydrogen bonding interaction between the proton of NH of substrates and the oxygen atom of the boryl moiety on the catalyst favors *ortho* selectivity[4].

Smith III *et al.* (*J. Am. Chem. Soc.* **2017**)



Smith III *et al.* (*Angew. Chem. Int. Ed.* **2013**)

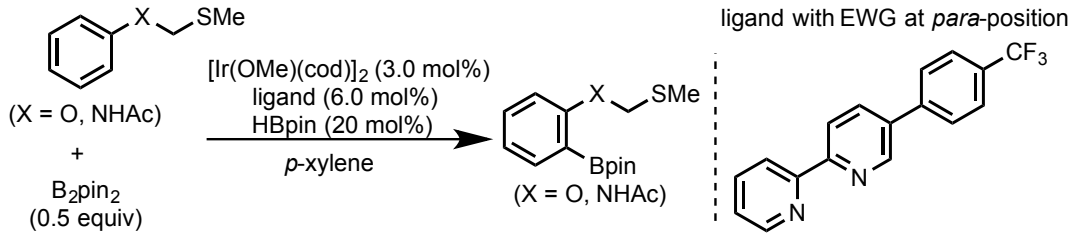


Scheme 3-2 Non-covalent bond interaction-controlled *ortho* C-H borylation

3.2 Iridium/Bipyridine Catalyzed *ortho*-Selective C-H Borylation of Phenol and Aniline Derivatives

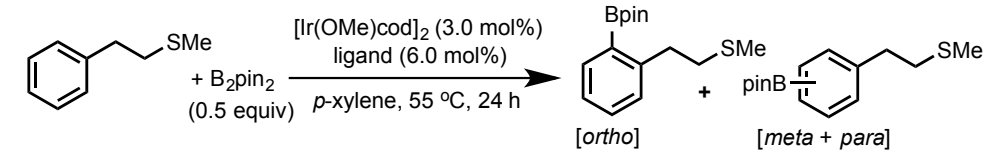
The *ortho* C-H borylation of phenols and anilines is more difficult than *ortho* C-H borylation of other aromatic substrates because hydroxy and amino groups will hamper borylation reaction. Therefore, a suitable protecting group is very important for this kind of reaction. In those precedent examples, alkyl hydrosilyl and Bpin were successfully used as protecting groups. They can be easily removed under mild conditions. Herein I developed a new *ortho*-selective C-H borylation of phenol and aniline derivatives by protecting hydroxy and amino group using methylthiolmethlene (-CH_2SCH_3, MTM) and simply introducing an electron withdrawing group on the bipyridine type ligand.

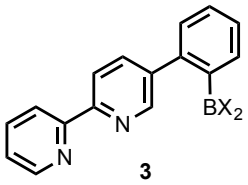
Figure 3.1 The *ortho*-selective C-H borylation of phenols and anilines



After development of *ortho* C-H borylation of aryl sulfides, I tried to further expand substrates scope of this reaction. First, I investigated a substrate with a two-carbon linker between sulfur atom and benzene ring by using bipyridine type **ligand 3** with a Lewis acidic group at *ortho*-position and dtbpy. The results are shown in **Table 3.1**. The C-H borylation proceeded in good yield with high *ortho*-selectivity using **ligand 3d**, whereas, the [*ortho*/(*meta* + *para*)] ratio in dtbpy case was very low. In entry 2, borylation reaction did not proceed using **ligand 3c** bearing four trifluoromethyl groups in the 1,3,2-dioxaborolanyl group. Inspired by this good result, I thought that the *ortho* C-H borylation can be applied to phenol and aniline substrates by protecting the hydroxy and amino groups using methylthiolmethlene (-CH_2SCH_3, MTM).

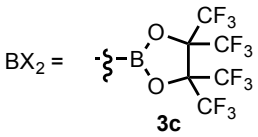
Table 3.1 *ortho*-Selective C-H borylation of methyl(phenethyl)sulfane



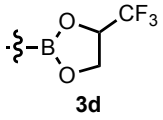


3

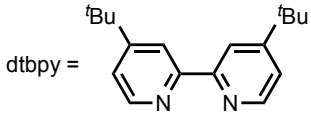
entry	ligand	yield / %	Ratio [o : (*m*+*p*)]
1	dtbpy	71	1.4 : 1
2	3c	< 1	—
3	**3d**	**77**	**>20 : 1**



3c



3d

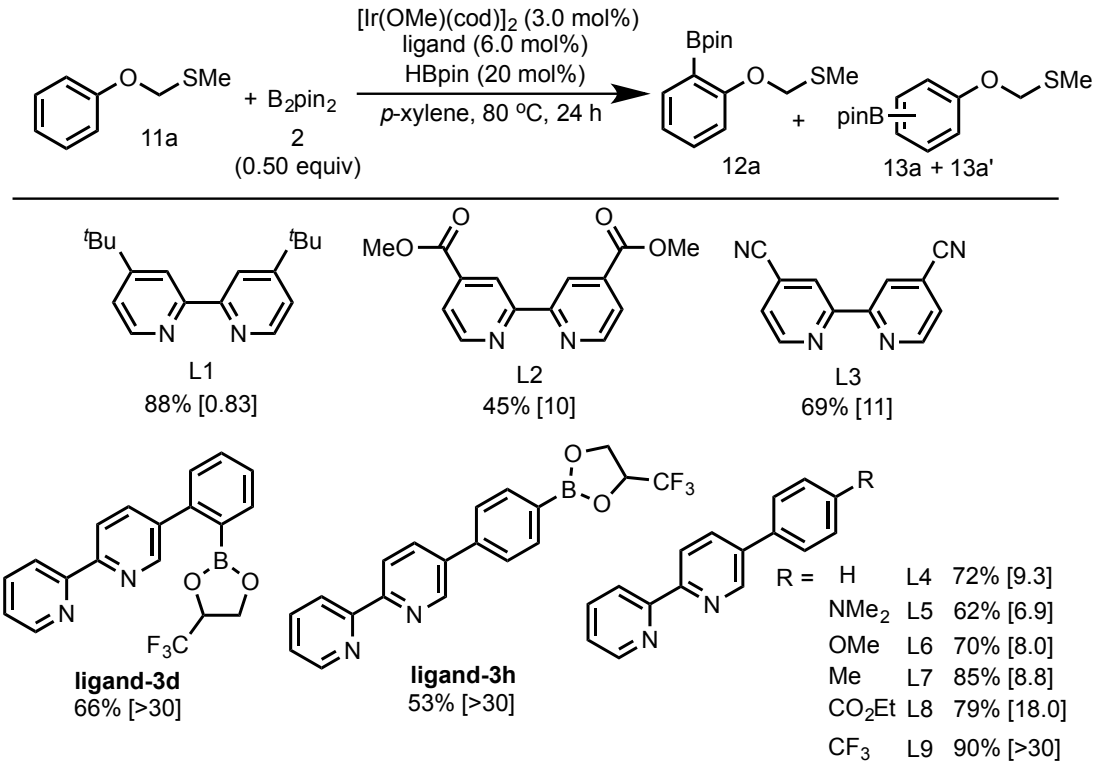


3.2.1 Ligand screening of *ortho*-selective C-H borylation of phenols substrates

First, I investigated several symmetric bipyridine type ligands in a reaction between phenol substrate **11a** and bis(pinacolato)diboron (**2**) (**Table 3.2**). Ligand **L1** (dtbpy) gave a mixture of *ortho*-, *meta*-, and *para*-C-H borylated products in 88% yield, but the [*ortho*/(*meta* + *para*)] ratio was low (0.83). Compared with dtbpy case, the [*ortho*/(*meta* + *para*)] ratio was improved using bipyridine ligands **L2-L3** with electron-withdrawing groups, but the yield of C-H borylated products decreased. One possibility to account for the decreased yields is that electron-withdrawing effects on bipyridine ligand are unfavorable for ligand-iridium coordination. The [*ortho*/(*meta* + *para*)] ratio was dramatically improved using **ligand 3d** bearing one trifluoromethyl group-substituted 1, 3,2-dioxaborolanyl group at *ortho* position. More interestingly, the borylation reaction also occurred with high *ortho* selectivity using **ligand 3h** with one trifluoromethyl groups substituted 1,3,2-dioxaborolanyl group at *para* position, but the yield of borylated products was still unsatisfactory in these two cases. These results suggested that the key activating and controlling element for *ortho* C-H borylation of phenol substrate was related to electronic property of bipyridine ligand instead of Lewis acid-base interaction between ligand and substrate. In order to gain preliminary insight into

electronic property of ligand effect on *ortho*-selectivity, I started to screen a series of asymmetric bipyridine ligands with different electronic properties[5]. When using 5-phenyl-2,2'-bipyridine (**L4**) as a ligand, a mixture of C-H borylated products was afforded in 57% yield with [*ortho*/(*meta* + *para*)] in 6.0. Several substituents at *para* position of bipyridine ligands were screened to improve the yield and the ratio. I found, the increased electron-withdrawing ability of the substituent enhanced the yield and the [*ortho*/(*meta* + *para*)] ratio, and trifluoromethylated ligand **L9** gave the best result in 90% yield with [*ortho* / *meta* + *para*] ratio over 30.

Table 3.2 Ligand effect on *ortho*-selective C-H borylation of phenol substrates



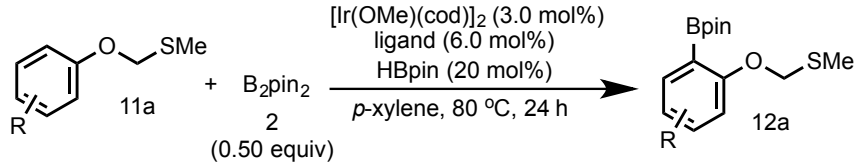
[a] The yield is a total yield of *ortho*-, *meta*-, and *para*-products.
[b] The [*ortho*/*meta* + *para*] ratios were shown in square brackets.

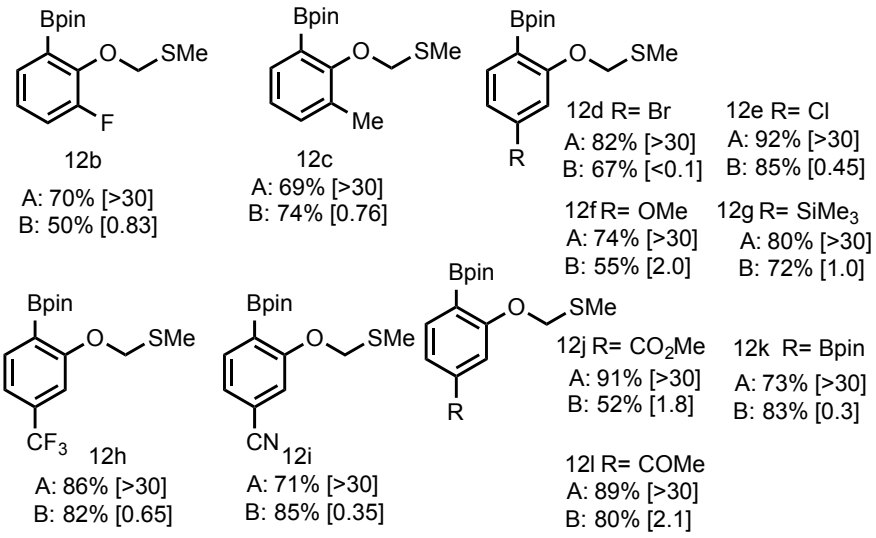
3.2.2 Substrates scope of this *ortho*-selective C-H borylation reaction [6]

Under the best conditions, I began to investigate the substrate scope of this *ortho* selective C-H borylation reaction (**Table 3.3-3.4**). Using phenol derivatives as substrates, the *ortho*-selectivity in all entries was dramatically improved using ligand **L9** compared with dtbpy. The desired *ortho*-C-H borylation proceeded in good to excellent yield by introducing an electron-withdrawing or -donating substituent at the *ortho*-position and *meta*-position of the benzene ring in the case of **11b-11l**. There are two possible reaction sites in the case of phenol substrates with a substituent at the *meta*-position. The C-H borylation proceeded only at the *ortho*-position with less steric hindrance and gave *ortho*-borylated products **12d-12l** without loss of the functional groups.

The *ortho*-selective C-H borylation also occurred very well using aniline derivatives **11m-11t** and gave the corresponding *ortho*-borylated products **12m-12t** in good yield without inhibition by the functional groups and/or loss of the functional groups. In the case of substrate **11t** with a cyano substituent at *meta*-position, it can give di-ortho-borylated product even at the sterically hindered *ortho*-position. However, the C-H borylation will give poor *ortho*-selectivity when protecting the hydroxy or amino group using methoxylmethlene (-CH_2OCH_3, MOM) to replace methylthiolmethlene (-CH_2SCH_3, MTM) such as using (methoxymethoxy)benzene as substrate (**L9**: 61% [*ortho*/(*meta* + *para*) <0.01]; dtbpy: 50% [*ortho*/(*meta* + *para*) <0.01]). Interestingly, the yield of borylated products and the [*ortho*/(*meta* + *para*)] ratio were improved using electron poor ligand compared with dtbpy in many entries. The result indicated that the sulfur atom at the γ-position and ligand with electron withdrawing group are important to control the *ortho*-regioselectivity.

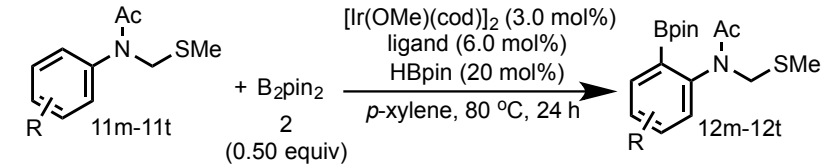
Table 3.3 Substrates scope for *ortho* C-H borylation of phenol derivatives

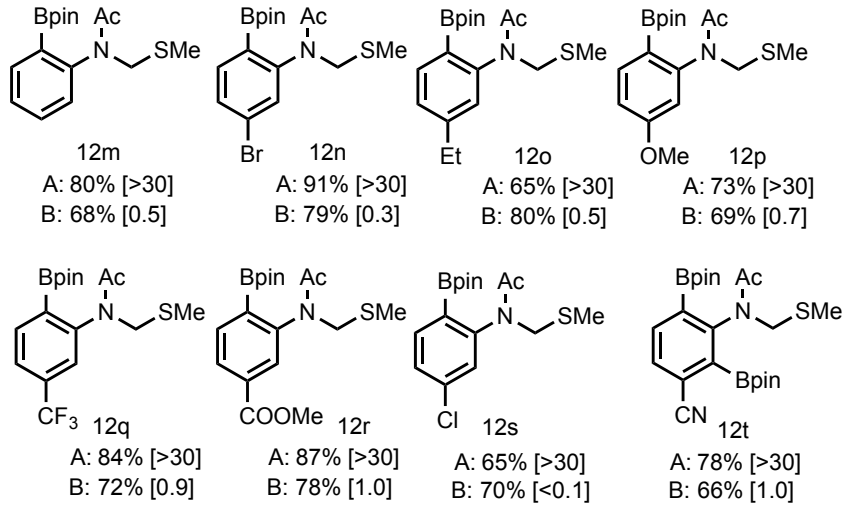




[a] 2a (0.50 equiv). The yield is a total yield of *ortho*-, *meta*-, and *para*-products.
[b] A : Ligand case, [*ortho*/*meta* + *para*] ratios. [c] B : dtbpy case, [*ortho*/*meta* + *para*] ratios

Table 3.4 Substrates scope for ortho C-H borylation of aniline derivatives

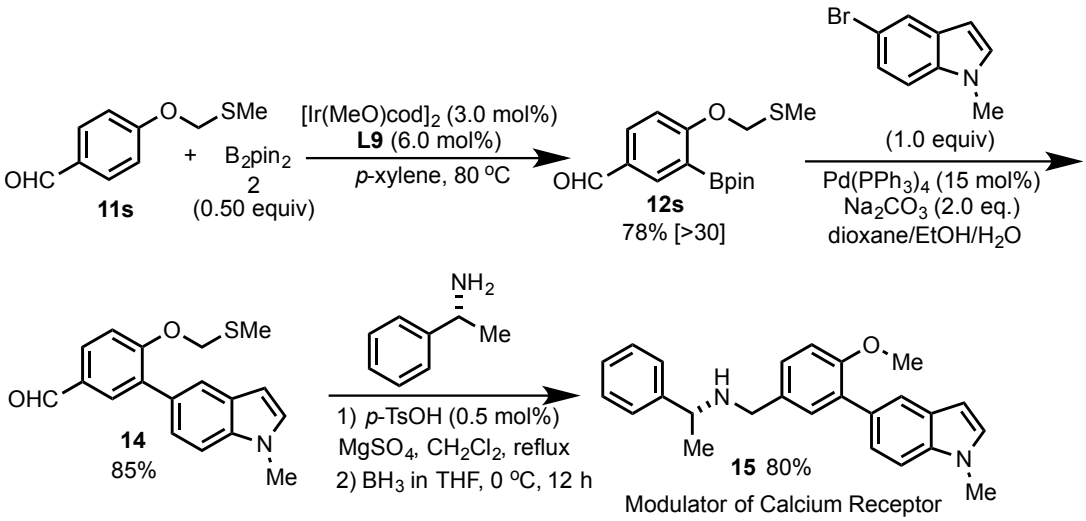




[a] 2a (0.50 equiv). The yield is a total yield of *ortho*-, *meta*-, and *para*-products.
[b] A : Ligand case, [*ortho*/*meta* + *para*] ratios. [c] B : dtbpy case, [*ortho*/*meta* + *para*] ratios

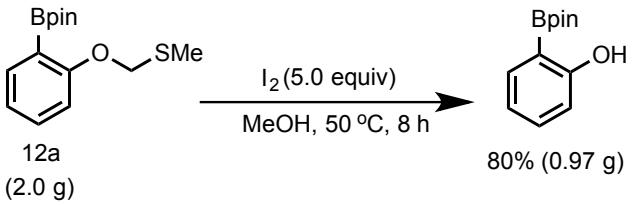
3.2.3 Application and deprotection reaction[7-10]

To demonstrate the utility of this *ortho* C-H borylation, I tried to synthesize the modulator of calcium receptor **15** through the following three steps. Using MTM-protected *para*-hydroxybenzaldehyde as starting material, the desired borylation reaction proceeded in good yield and regioselectively, introducing Bpin at *ortho*-positon of the hydroxyl substituent. Then, *ortho*-borylated product **12s** coupled with 5-bromo-1-methyl-1*H*-indole to generate **14** in 85% yield. The last step is a one-pot reaction in which imine formation occurred between intermediate **14** and (*R*)-1-phenylethan-1-amine followed by reduction using BH_3 in THF. It is notable that the MTM protecting group was reduced to methyl at the same time.



Scheme 3-3 The synthetic route of bioactive compound **15**

In addition, I also investigated some experiments to removal the MTM protecting group. The I_2/MeOH system showed extremely efficient capability of removing the MTM group in good yield, even in gram scale[11].



Scheme 3-4 Method for removing MTM protecting group

3.2.4 Proposed mechanism of this *ortho* C-H borylation

According to experimental results, I proposed two possible mechanisms of this reaction. (1) via outer-sphere Lewis acid-base interaction between a boryl ligand of an iridium center and a sulfur atom of a substrate (**Figure 3.2**, 1)); (2) via coordination of a sulfur atom of a substrate to an iridium center as a directing group-assisted process (**Figure 3.2**, 2)).

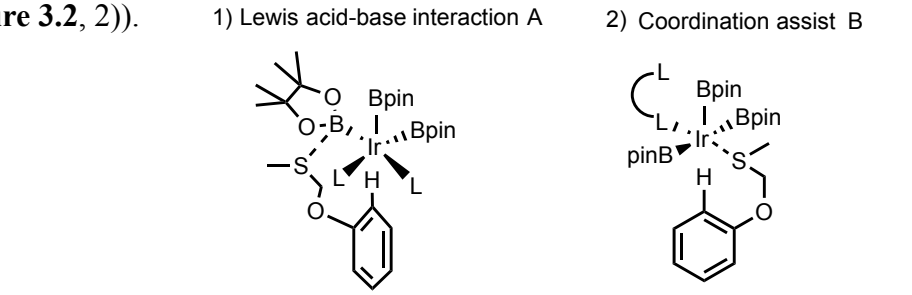
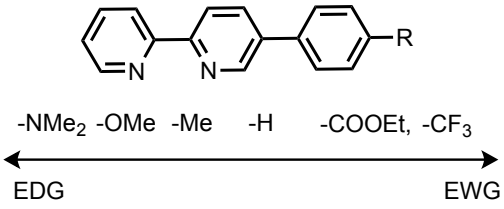


Figure 3.2 Two possible mechanisms of this *ortho* C-H borylation

Evidence for mechanism A: an experimental result supporting Lewis acid-base interaction between substrate and catalyst is the observation that the *ortho*-selectivity was consistent with the acidity of bipyridine ligands. For example, increased acidity of ligand from **L5** to **L9** dramatically enhanced *ortho*-selectivity (**Figure 3.3**). I proposed electron-poor ligand could increase Lewis acidity of the boron atom in the iridium boryl complex, which accounts for the increased *ortho*-selectivity[12]. However, the effect of electronic property of substrate on the *ortho*-selectivity was not obvious. In the case of substrate **12q** with a strong EWG (-CF_3) at *meta* position also gave high *ortho*-selectivity. One possible reason for this result is that the distance between the sulfur atom of MTM group and the benzene ring made the trifluoromethyl substituent weak impact on sulfur atom.



Electronic effect on the ratio

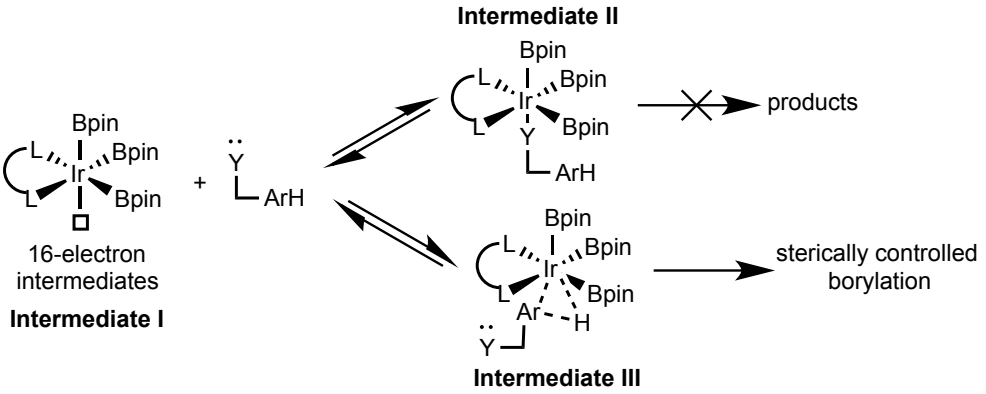
ligand	R	yield / %	[*o* : (*m*+*p*)]
L9	CF_3	90%	>30
L8	COOEt	79%	18
L7	Me	85%	8.8
L6	OMe	70%	8.0
L5	NMe_2	62%	6.9

Figure 3.3 The effect of electronic property of ligand on *ortho*-selectivity

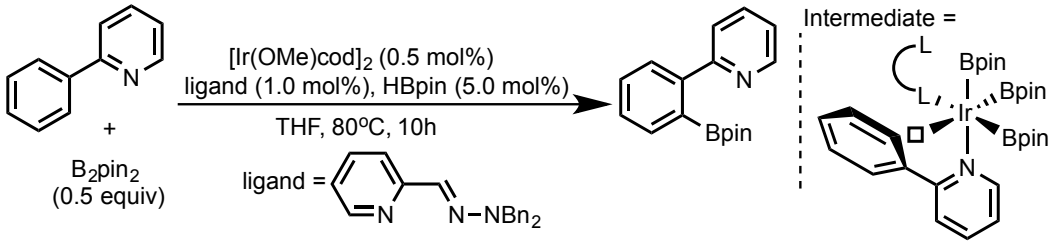
Evidence for mechanism B: Usually, the iridium/bipyridine-catalyzed C-H borylation reaction proceeds through a 16-electron intermediate **I**, which only contains one coordination site. The directing atom Y coordinating with intermediate **I** can not give borylated product. As a result, the activation of arene C-H bonds can only proceed through intermediate-III and the regioselectivity is therefore mainly controlled by steric hindrance (**Figure 3.4** (1)). On the other hand, the *ortho* C-H borylation of phenol and aniline derivatives made me to envision that such a reaction would require to regenerate an additional coordination site during the reaction. This idea has been confirmed by Lassaletta in 2011. He developed an *ortho*-selective C-H borylation of 2-phenylpyridine using a designed ligand, in which the two nitrogen atom has different coordination ability to iridium center and one of them could dissociate from iridium during reaction (**Figure 3.4** (2)). Thus, I propose that the existence of trifluoromethyl group at *para*-position makes the two nitrogen atom of **L9** have different coordination ability to iridium, which results in *ortho*-selectivity[13].

In order to prove this hypothesis, I also investigated this reaction by using the following two *mono*-dentate ligands (**Figure 3.4** (3): **L10**, **L11**). Both of them afforded high [*ortho*/(*meta* + *para*)] ratio, which can be view as a potential evidence to support mechanism B.

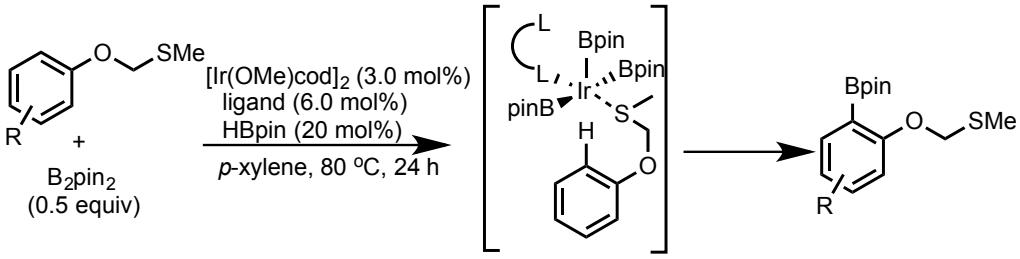
(1) Mechanism for Ir(III)/bipyridine catalyzed borylation

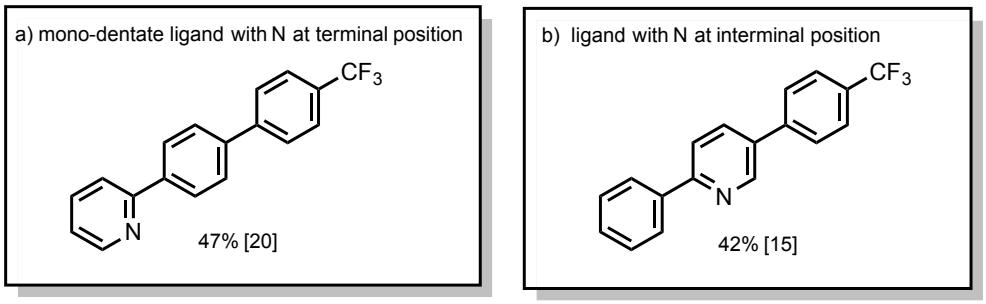


(2) Lassaletta M. *et al.* (*Angew. Chem. Int. Ed.* 2011)



(3) *mono*-Dentate ligands applied into the reaction





[a] The yield is a total yield of *ortho*-, *meta*-, and *para*-products. [b] [*ortho*/*meta* + *para*] ratios are shown in the square brackets

Figure 3.4 Some evidences for supporting mechanism B

3.3 Summary

In summary, I successfully developed *ortho*-selective C-H borylation of phenol and aniline derivatives by introducing an MTM group on the hydroxyl and amino substituents and using a bipyridine-type ligand with an electron-withdrawing group. The protecting group of phenol and aniline derivatives can be easily removed under mild conditions, even in gram-scale. The reaction also proceeded in high yields and *ortho*-regioselectivity with good functional group tolerance. The *ortho*-selective C-H borylation was applied to the synthesis of a bioactive compound. Even though the mechanism of this reaction has not been clarified at present, it is confirmed that the *ortho*-selectivity is related to the electronic property of bipyridine ligand. I hope that my research could provide a new view for the development of regioselective C-H borylation reaction.

References

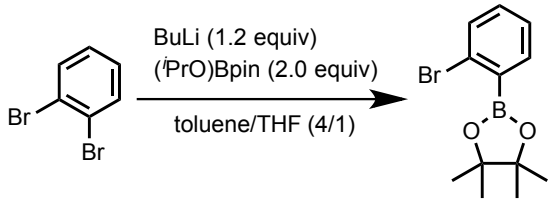
1. Tyman, H. P.; Synthetic and Natural Phenols, Elsevier, Amsterdam, **1996**.
2. a) Abrecht, W.; Neumann, H.-G. *Arch. Toxicol.* **1985**, *57*, 1; b) Briner, G.; Neumann, H. –G. *Arch. Toxicol.* **1988**, *62*, 110; c) Lester, D. *J. Pharmacol. Exp. Ther.* **1943**, *77*, 154; d) Jenkins, F. P. *et al. Fd. Cosmet. Toxicol.* **1972**, *10*, 671.
3. Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 7534.
4. a) Chattopadhyay, B.; Dannatt, J. E.; Sanctis, I. L. A.; Gore, K. A.; Maleczka, R. E. Singleton, D. A.; Smith, M. R. *J. Am. Chem. Soc.* **2017**, *139*, 7864; b) Preshlock, S. M.; Plattner, D. L.; Maligres, P. E.; Krska, S. W.; Maleczka Jr, R. E.; Smith III, M. R. *Angew. Chem. Int. Ed.* **2013**, *52*, 12915.
5. For the preparation of bipyridine type of ligands, see examples: a) Mahata, K.; Frischmann, P. D.; Würthner, F. *J. Am. Chem. Soc.* **2013**, *135*, 15656; b) Wang, Y. J.; Chang, G.; Chen, Q.; Yang, G. J.; Fan, S. Q.; Fang, B.; *Chem. Commun.* **2015**, *51*, 685; c) Beinhoff, M.; Weigel, W.; Jurczok, M.; Retting, W.; Modrakowski, C.; Brüdgam, I.; Hart, H.; Schlüter, A. D. *Eur. J. Org. Chem.* **2001**, 3819.
6. For the preparation of substrates, see: a) Holton, R. A.; Davis, R. G. *Tetrahedron Lett.* **1977**, *6*, 533; b) Vo. C. V. T.; Mitchell, A.; Bode, J. W. *J. Am. Chem. Soc.* **2011**, *133*, 14082; c) Iwasaki, T.; Miyata, Y.; Akimoto, R.; Fujii, Y.; Kunigasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2014**, *136*, 9260.
7. Kelly-Michael, G.; Xu, S.; Xi, N.; Miller, P.; Kincaid, J. F.; Ghiron, C. Calcium receptor modulating arylalkylamines, WO 03099776, May 23, 2003.
8. Mahata, K.; Frischmann, P. D.; Würthner, F. *J. Am. Chem. Soc.* **2013**, *135*, 15656.
9. Goldeman, W.; Soroka, M. *Synthesis* **2010**, *14*, 2437.
10. a) Cho. B. T.; Kang, S. K. *Tetrahedron* **2005**, *61*, 5725. b) Nisanci, B.; Ganjehyan, K.; Metin, Ö.; Dastan, A.; Torok, B. *J. Molecul. Catal. A.* **2015**, *409*, 191.
11. Keith J. M. *Tetrahedron Lett.* **2004**, *45*, 2739.
12. We reported regioselective C-H reactions using Lewis acid-base interaction between substrates. See: a) Wakaki, T.; Kanai, M.; Kuninobu, Y. *Org. Lett.* **2015**, *17*, 1758; b) Murai, M.; Omura, T.; Kuninobu, Y.; Takai, K. *Chem. Commun.* **2015**, *51*, 4583;
13. Ros. A.; Estepa, B.; Lopez-Roriguez, L. Alvarez, E.; Fernandez, R.; Lassaletta, J. M. *Angew. Chem. Int. Ed.* **2011**, *50*, 11724

Experimental Sections

1. Development of *ortho*-Selective C-H Borylation of Aryl Sufides Controlled by Lewis Acid-Base Interaction

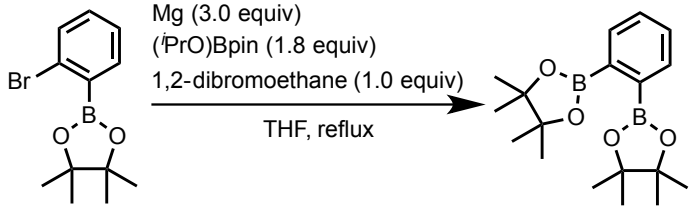
General. All reactions were carried out in a dry and degassed solvent under an argon atmosphere. Compounds **1a-1f**, **1j**, **1n**, **1o**, 1,2-dibromobenzene, diethylchlorothiophosphate 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 1,4-dibromobutane 3-(methylthiol)aniline Bis(2-bromoethyl)ether and diols including 2-methyl-2,4-pentanedol, 1,3-butanediol, 2,2-dimethyl-1,3-propanediol, 6-bromoindole, (±)-*N*,*N*,*N'*,*N'*-tetramethyltartardiamide, 3,3,3-trifluoro-1,2-propanediol, hexafluoro-2,3-bis(trifluoromethyl)-2,3-butanediol and 3-(methylthiol)phenol were purchased from Aldrich, Alfa Aesar, TCI, and Wako, and used without further purification unless otherwise noted. Compounds **1g**,[1] **1h**,[2] **1k**,[3] **1l**,[3] **1m**,[4] **1p**,[5] **1q**,[3] **1s**,[6] **1t**,[7] and **1u**[7] were prepared according to the literature methods. Reactions were monitored by thin-layer chromatography (TLC) visualizing with UV-light (254 nm). Organic solutions were concentrated under reduced pressure using a rotary evaporator (30 °C, <50 torr). NMR spectra were recorded on 500 MHz (500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR) and 400 MHz (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectrometers. Proton and carbon chemical shifts are reported relative to the solvent used as an internal reference. In ^{13}C NMR, signals of carbons adjacent to a boron atom were not observed because of the quadrupolar relaxation. Infrared (IR) spectra were recorded on Fourier transform infrared spectrophotometer. ESI-MS spectra were measured on a spectrometer for HRMS.

Synthesis of 2-(2-bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3a-1).



1,2-Dibromobenzene (1.5 mL, 2.90 g, 12.3 mmol) and (^{i}PrO)Bpin (4.9 mL, 4.58 g, 24.6 mmol) were dissolved in a mixture of toluene/THF (4/1, 150 mL), and the solution was cooled to −78 °C. A solution of BuLi in *n*-hexane (1.6 M, 17.4 mL, 27.9 mmol) was added dropwise with stirring over 3 h. After the addition, the solution was stirred for 4 h at −78 °C and then slowly warmed to room temperature and the mixture was stirred at room temperature overnight. The resulting suspension was treated with a saturated aqueous solution of $NaHCO_3$ (10 mL). After stirring for 10 min, separation of the organic and aqueous phases, then the aqueous phase was extracted with hexane (2 × 10 mL) and ethyl acetate (2 × 10 mL). The combined organic phase was washed with H_2O (50 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under vacuum and the pale yellow oily residue was distilled under reduced pressure (0.2 MPa, 120 ^{o}C) to give a colorless viscous liquid. Yield: 2.5 g (72.3%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 7.22-7.26 (m, 2H), 7.51-7.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.0, 84.5, 126.5, 128.2, 132.1, 132.9, 136.6.

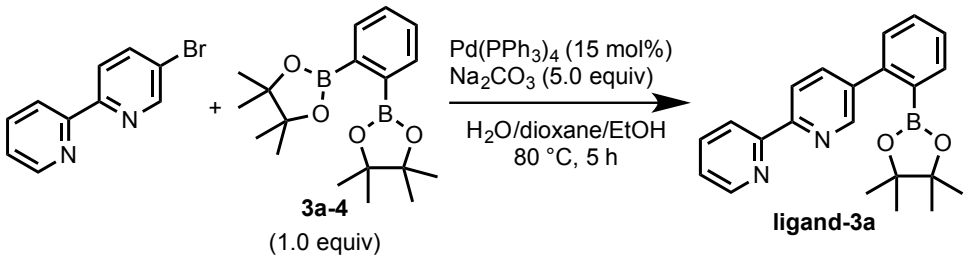
Synthesis of 1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzene(3a-4).



Mg turnings (1.52 g, 62.5 mmol) were heated under vacuum for 15 min in a two-necked flask equipped with a reflux condenser and a dropping funnel. After the flask was cooled to room temperature, 2-(2-bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.90 g, 20.9 mmol), (^{i}PrO)Bpin (7.9 mL, 7.30 g, 39.2 mmol), and THF (100 mL) were added. The mixture was heated at 70 ^{o}C for 30 min, and the oil bath was switched off and a solution of 1,2-dibromoethane (1.8 mL, 3.90 g, 20.8 mmol) in THF (10 mL) was added slowly to the reaction mixture at ca. 50 ^{o}C over 1 h. After the

addition, the solution was heated under reflux for 4 h. Then, the mixture was allowed to cool to room temperature and stirred overnight. The mixture was treated with a saturated aqueous solution of $NaHCO_3$ (30 mL) and stirred for 30 min, the two liquid phases were separated, and the aqueous phase was extracted with hexane (30 mL) and ethyl acetate (30 mL). The combined organic phases were washed with H_2O (30 mL), dried over anhydrous Na_2SO_4, filtered, and all volatiles were removed by filtration. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 10/1). The desired product was obtained as a colorless solid. Yield: 4.78 g (69%); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 24H), 7.36-7.38 (m, 2H), 7.63-7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ25.1, 84.1, 129.4, 133.7.

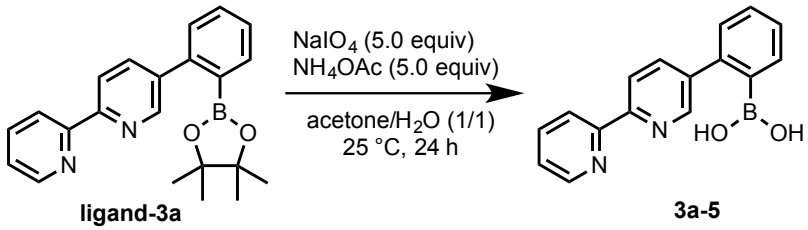
5-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-2,2'-bipyridine(3a).



Into a 50 mL two-necked flask quipped with a reflux condenser, 5-bromo-2,2'-bipyridine (1.00 g, 4.27 mmol), 1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzene(1.41 g, 4.27 mmol), $Pd(PPh_3)_4$ (745 mg, 0.640 mmol), and sodium carbonate (2.30 g, 21.5 mmol) were added. After addition of 1,4-dioxane (40 mL), EtOH (28 mL) and water (28 mL), the mixture was refluxed for 4 h. The reaction was cooled to room temperature and extracted with a mixture of EtOAc (20 mL) and hexane (20 mL). The two liquid phases were separated and the organic phase was washed with H_2O (50 mL), and dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed under vacuum to give yellow oil crude product, which was purified by column chromatography on silica gel (hexane/EtOAc = 10/1). The target compound was obtained as a colorless solid. Yield: (1.1 g, 70%); white solid (mp. 112-115 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 12H), 7.30-7.33 (m, 1H), 7.39-7.43 (m, 2H), 7.50-7.52 (m, 1H), 7.81-7.86 (m, 3H), 8.40-8.46 (m, 2H), 8.69-8.71 (m, 2H); ^{13}C

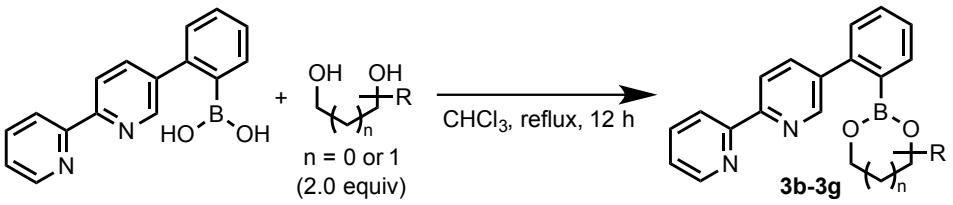
NMR (100 MHz, $CDCl_3$) δ 24.9, 84.2, 120.1, 121.3, 123.8, 127.4, 129.5, 130.9, 135.7, 137.1, 137.6, 138.9, 144.3, 149.4, 149.6, 154.7, 156.5; IR (KBr, ν / cm^{-1}) 2973, 1594, 1431, 1348, 1269, 1146, 859, 766, 662; HRMS (ESI^+) Calcd for $C_{22}H_{23}BN_2O_2H$ ($[M+H]^+$) 359.1925, Found 359.1921.

Synthesis of 2-(2,2'-bipyridin-5-yl)phenylboronic acid.



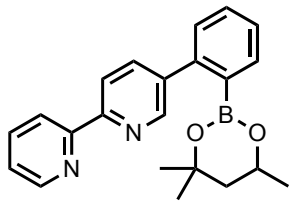
5-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-2,2'-bipyridine (**3a**, 1.00 g, 2.79 mmol), NH_4OAc (1.08 g, 14.0 mmol), $NaIO_4$ (2.98 g, 14.0 mmol), and a mixture of acetone and H_2O (1/1) were added into a one-necked round-bottom flask. The mixture was stirred at room temperature for 24 h, then the reaction mixture was extracted with EtOAc (15 mL). The organic phase was dried over Na_2SO_4, filtered, and the solvent was removed under vacuum. As a result, the target compound was obtained as a light yellow powder (mp. 121-123 ^oC). Yield: (10.6 mg, 70%); ^1H NMR (400 MHz, CD_3OH) δ 7.43-7.55 (m, 5H), 7.94-8.00 (m, 2H), 8.36-8.40 (m, 2H), 8.66-8.69 (m, 2H); ^{13}C NMR (100 MHz, CD_3OH) δ 123.2, 123.5, 126.3, 129.6, 130.4, 131.5, 134.6, 138.8, 139.7, 141.5, 143.0, 150.2, 151.2, 156.8, 157.7; IR (KBr, ν / cm^{-1}) 3166, 1592, 1463, 1433, 1381, 1149, 1028, 860, 762; HRMS (ESI^+) Calcd for $C_{16}H_{13}BN_2O_2H$ ($[M+H]^+$) 277.1143, Found 277.1151.

Synthesis of ligands 3b-3g.



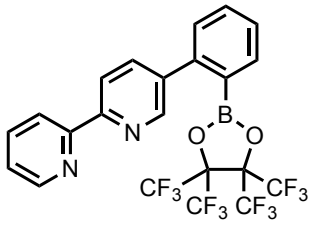
2-(2,2'-Bipyridin-5-yl)phenylboronic acid (100 mg, 0.360 mmol) and diol (2.0 equiv) were dissolved in chloroform (20 mL) in a round-bottom flask, and the mixture was refluxed for 12 h. After removal of the solvent, the yellow oil crude product was purified by column chromatography on silica gel (hexane/toluene/EtOH = 10/1/1).

5-(2-(4,4,6-Trimethyl-1,3,2-dioxaborinan-2-yl)phenyl)-2,2'-bipyridine (3b).



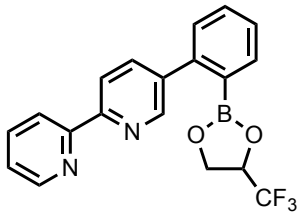
Yield: 80%; white solid (mp. 80-82 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08-1.09 (m, 6H), 1.21 (s, 3H), 1.46-1.53 (m, 1H), 1.72 (dd, *J* = 14.2, 3.2 Hz, 1H), 4.16-4.21 (m, 1H), 7.29-7.40 (m, 3H), 7.43-7.47 (m, 1H), 7.79-7.84 (m, 3H), 8.39-8.44 (m, 2H), 8.68-8.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 28.1, 31.1, 46.0, 65.5, 71.6, 120.1, 121.2, 123.7, 127.4, 129.4, 129.9, 134.5, 137.1, 137.2, 140.0, 143.5, 149.4, 149.5, 154.2, 156.6; IR (KBr, ν / cm^{-1}) 2972, 1588, 1457, 1301, 1167, 801, 750, 649; HRMS (ESI^+) Calcd for $C_{22}H_{23}BN_2O_2H$ ($[M+H]^+$) 359.1925, Found 359.1909.

5-(2-(4,4,5,5-Tetrakis(trifluoromethyl)-1,3,2-dioxaborolan-2-yl)phenyl)-2,2'-bipyridine (3c).



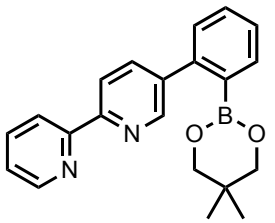
Yield: 78%; yellow solid (mp. 168-170 ^{o}C); ^{1}H NMR (400 MHz, CD_3OH) δ 7.19-7.21 (m, 1H), 7.28-7.32 (m, 2H), 7.66-7.69 (m, 1H), 7.79 (d, *J* = 6.8 Hz, 1H), 8.14-8.18 (m, 1H), 8.41 (d, *J* = 8.2 Hz, 1H), 8.57-8.60 (m, 2H), 8.87-8.90 (m,2H); ^{13}C NMR (100 MHz, CD_3OH) δ 124.3, 124.5 (q, *J* = 306 Hz), 124.6, 128.1, 128.6, 129.3, 130.4, 136.6, 139.7, 141.2, 144.7, 147.1, 148.0, 148.2, 149.3, 151.7 [Two quaternary aliphatic carbons could not be detected.]; IR (KBr, ν / cm^{-1}) 1544, 1464, 1227, 1166, 963, 878, 795, 754, 713; HRMS (ESI^+) Calcd for $C_{22}H_{11}BF_{12}N_2O_2Na$ ($[M+Na]^+$) 597.0614, Found 597.0625.

5-(2-(4-(Trifluoromethyl)-1,3,2-dioxaborolan-2-yl)phenyl)-2,2'-bipyridine (3d).



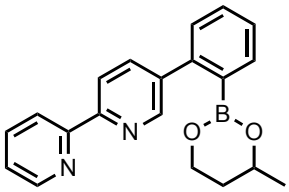
Yield: 70%; pink oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27-4.35 (m, 2H), 4.69-4.71 (m, 1H), 7.34-7.35 (m, 1H), 7.41-7.48 (m, 2H), 7.58-7.60 (m, 1H), 7.80-7.85 (m, 2H), 7.96 (d, *J* = 7.3 Hz, 1H), 8.41-8.46 (m, 2H), 8.67-8.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.9, 74.3 (q, *J* = 34.3 Hz), 120.5, 121.6, 123.9 (q, *J* = 284 Hz), 124.0, 127.7, 130.0, 132.1, 136.7, 137.4, 137.8, 138.6, 145.2, 149.1, 149.4, 154.7, 156.0; IR (KBr, ν / cm^{-1}) 1591, 1462, 1432, 1381, 1147, 801, 754; HRMS (ESI^+) A target mass was not detected due to decomposition of **3d**.

5-(2-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)phenyl)-2,2'-bipyridine (3e).



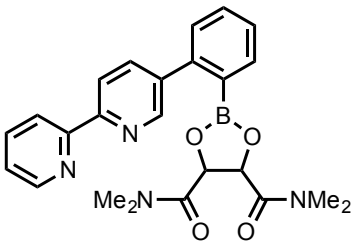
Yield: 73%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (s, 6H), 3.55 (s, 4H), 7.29-7.30 (m, 1H), 7.36-7.40 (m, 2H), 7.46-7.48 (m, 1H), 7.80-7.85 (m, 3H), 8.39 (d, *J* = 8.2Hz, 1H), 8.43 (dd, *J* = 8.2 Hz, 1H), 8.70-8.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 31.8, 72.4, 120.1, 121.3, 123.7, 127.4, 129.6, 130.2, 134.8, 137.1, 137.3, 139.7, 143.6, 149.3, 149.4, 154.4, 156.5; IR (KBr, ν / cm^{-1}) 2961, 1589, 1457, 1303, 1134, 801, 766, 650; HRMS (ESI^+) A target mass was not detected due to decomposition of **3e**.

5-(2-(4-Methyl-1,3,2-dioxaborinan-2-yl)phenyl)-2,2'-bipyridine (3f).



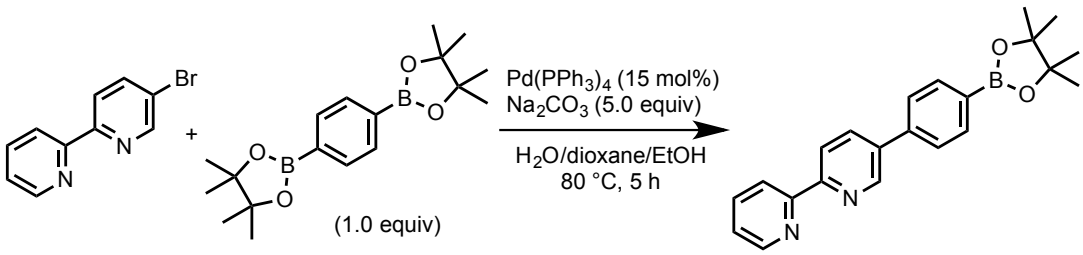
Yield: 65%; yellow solid (mp. 95-97 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05-1.07 (m, 3H), 1.68-1.71 (m, 1H), 1.87-1.90 (m,1H), 3.94-4.08 (m, 2H), 4.09-4.10 (m, 1H), 7.28-7.32 (m, 1H), 7.34-7.41 (m, 2H), 7.44-7.48 (m, 1H), 7.79-7.84 (m, 3H), 8.39-8.44 (m, 2H), 8.69-8.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7, 34.3, 61.6, 68.0, 120.2, 121.2, 123.7, 127.3, 129.5, 130.0, 134.6, 137.1, 137.2, 139.8, 143.5, 149.4, 149.5, 154.3, 156.5; IR (KBr, ν / cm^{-1}) 1589, 1457, 1364, 1303, 1138, 769, 752, 648; HRMS (ESI^+) A target mass was not detected due to decomposition of **3c**.

2-(2-(2,2'-Bipyridin-5-yl)phenyl)-*N*4,*N*4,*N*5,*N*5-tetramethyl-1,3,2-dioxaborolane-4,5-dicarboxamide (3g).



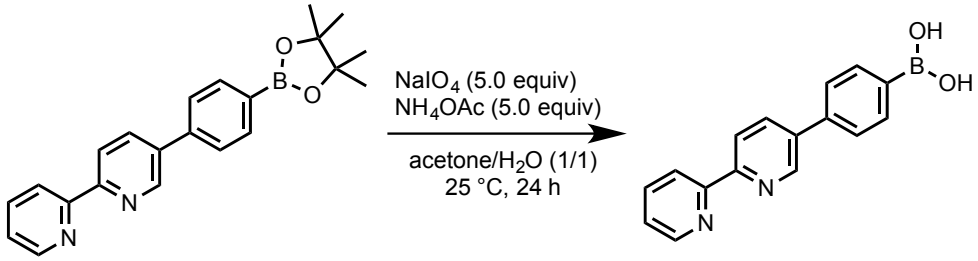
Yield: 53%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.89 (s, 12H), 5.61 (s, 2H), 7.33-7.43 (m, 3H), 7.56-7.58 (m, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.82-7.86 (m, 1H), 7.95 (d, *J* = 7.8Hz, 1H), 8.39-8.45 (m, 2H), 8.65-8.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.1, 37.0, 76.3, 120.1, 121.1, 123.9, 127.5, 129.8, 131.8, 136.7, 137.2, 137.7, 139.0, 145.3, 149.4, 149.5, 154.6, 156.2, 168.0; IR (KBr, ν / cm^{-1}) 3305, 1634, 1373, 1155, 862, 758, 640; HRMS (ESI^+) A target mass was not detected due to decomposition of **3g**.

5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-2,2'-bipyridine.



Into a 250 mL two-necked flask equipped with a reflux condenser, 5-bromo-2,2'-bipyridine (1.99 g, 8.54 mmol), 1,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzene (2.81 g, 8.54 mmol), $Pd(PPh_3)_4$ (1.50 g, 1.28 mmol), sodium carbonate (4.55 g, 42.9 mmol),1,4-dioxane (60 mL), EtOH (36 mL), and H_2O (36 mL) were added. Then the mixture was refluxed for 4 h. The reaction mixture was cooled to room temperature and extracted with a mixture of EtOAc (50 mL) and hexane (50 mL). The two liquid phases were separated, the organic phase was washed with H_2O (50 mL), and dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed under vacuum to give a yellow oil crud product, which was purified by column chromatography on silica gel (hexane/EtOAc = 10/1). The target compound was obtained as a colorless solid. Yield: 2.5 g, (80%); white solid (mp. 144-146 ^oC); ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 7.32-7.33 (m, 1H), 7.66 (d, J = 8.2 Hz, 2H), 7.83-7.86 (m, 1H), 7.93 (d, J = 8.2 Hz, 2H), 8.04-8.06 (m, 1H), 8.43-8.49 (m, 2H), 8.70-8.71 (m, 1H), 8.93-8.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.1, 84.2, 121.2, 121.3, 123.9, 126.6, 135.5, 135.8, 136.5, 137.2, 140.4, 147.9, 149.5, 155.4, 156.1; IR (KBr, ν / cm^{-1}) 2986, 1957, 1611, 1019, 963, 839, 799, 755, 660; HRMS (ESI^+) Calcd for $C_{22}H_{23}BN_2O_2H$ ($[M+H]^+$) 359.1925, Found 359.1908.

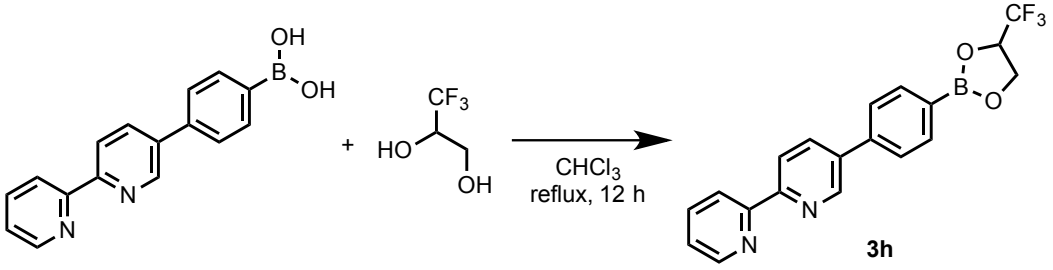
Synthesis of 4-(2,2'-bipyridin-5-yl)phenylboronic acid.



5-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-2,2'-bipyridine (500 mg,

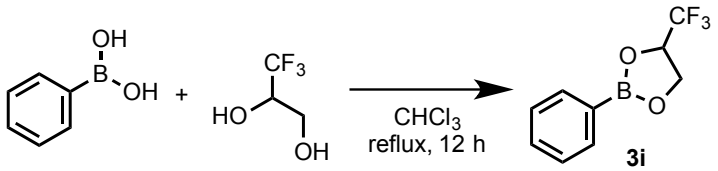
1.81 mmol), NH_4OAc (697 mg, 9.05 mmol), $NaIO_4$ (1.94 g, 9.05 mmol), and a mixture of acetone and H_2O (1/1) were added into a one-necked round-bottom flask, and the mixture was stirred at room temperature for 24 h. Then, the reaction mixture was extracted with EtOAc (35 mL). The organic phase was dried over Na_2SO_4, filtered, and the solvent was removed under vacuum to give the target compound as a light yellow powder (mp.178-180 ^oC). Yield: 61.6 mg (79%); ^1H NMR (400 MHz, CD_3OH) δ 7.43-7.46 (m, 1H), 7.71-7.97 (m, 5H), 8.18-8.20 (m, 1H), 8.35-8.39 (m, 2H), 8.66-8.67 (m, 1H), 8.92 (s, 1H); ^{13}C NMR (100 MHz, CD_3OH) δ 123.4, 123.5, 126.2, 128.0, 136.4, 136.7, 137.6, 138.9, 139.6, 149.3, 151.1, 156.8, 157.7; IR (KBr, ν / cm^{-1}) 3351, 1608, 1370, 795, 752, 638; HRMS (ESI^+) Calcd for $C_{16}H_{13}BN_2O_2H$ ($[M+H]^+$) 277.1143, Found 277.1132.

5-(4-(4-(trifluoromethyl)-1,3,2-dioxaborolan-2-yl)phenyl)-2,2'-bipyridine (3h).



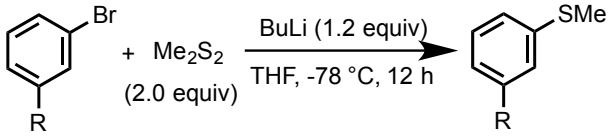
4-(2,2'-Bipyridin-5-yl)phenylboronic acid (50.0 mg, 0.180 mmol) and 3,3,3-trifluoropropane-1,2-diol (46.8 mg, 0.360 mmol) were dissolved in chloroform (20 mL) in a round-bottom flask, and the mixture was refluxed for 12 h. After removal of the solvent, a yellow oil crude product was purified by column chromatography on silica gel (hexane/toluene/EtOH = 10/1/1). The target compound was obtained as a colorless oil. Yield: 44.6 mg (67%); ^1H NMR (400 MHz, CD_3OH) δ 3.58-3.75 (m, 2H), 3.90-4.10 (m, 1H), 7.40-7.50 (m, 1H), 7.60-8.10 (m, 5H), 8.20-8.30 (m, 1H), 8.35-8.50 (m, 2H), 8.58-8.72 (m, 1H), 8.90-9.05 (m, 1H); ^{13}C NMR (100 MHz, CD_3OH) δ 62.5, 72.9 (q, J = 29.6 Hz), 123.4, 123.5, 125.9, 126.2, 127.2 (q, J = 287 Hz), 128.0, 136.4, 136.7, 137.6, 139.6, 149.4, 151.2, 156.8, 157.7; IR (KBr, ν / cm^{-1}) 3052, 1591, 1462, 1432, 1381, 1262, 1147, 801, 754; HRMS (ESI^+) A target mass was not detected due to decomposition of **3h**.

Synthesis of 2-phenyl-4-(trifluoromethyl)-1,3,2-dioxaborolane (3i).



Phenyl boronic acid (70.0 mg, 0.570 mmol) and 3,3,3-trifluoropropane-1,2-diol (149 mg, 1.15 mmol) were dissolved in chloroform (25 mL) in a round-bottom flask, and the mixture was refluxed for 12 h. After removal of the solvent, a crude product (yellow oil) was purified by column chromatography on silica gel (hexane/toluene/EtOH = 10/1/1). The target compound was obtained as a colorless oil. Yield: 98.4 mg (80%); ^{1}H NMR (400 MHz, CD_3OH) δ 4.44-4.55 (m, 2H), 4.84-4.90 (m, 1H), 7.40-7.44 (m, 2H), 7.51-7.55 (m, 1H), 7.84 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, CD_3OH) δ 65.9, 74.8 (q *J* = 34.3 Hz), 124.1 (q, *J* = 284 Hz), 128.2, 132.5, 135.4; IR (KBr, ν / cm^{-1}) 3077, 2964, 1965, 1602, 1493, 1353, 800, 700; HRMS (ESI^{+}) A target mass was not detected due to decomposition of **3i**.

General procedure for the preparation of aryl sulfides 1k-1m, 1q, and 1r.

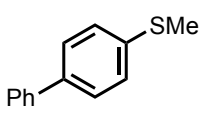


1k-**1m**, **1q**, and **1r**

To a solution of *m*-substituted bromobenzene (0.500 mmol) in THF (15.0 mL), *n*-BuLi (0.600 mmol, 1.2 equiv) was added dropwise at -78 °C under an argon atmosphere. After stirring for 30 min at the same temperature, a solution of dimethyl disulfide in 8.0 mL of THF (0.600 mmol, 1.2 equiv) was added dropwise. The mixture was then stirred for 4 h and slowly warmed to room temperature. After removal of the solvent under vacuum, the mixture was extracted with EtOAc. The organic layer was separated, dried over Na_2SO_4, filtered, and the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 10/1).

Biphenyl-4-yl(methyl)sulfane (1g).

Yield: 53%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (s, 3H), 7.32-7.34 (m, 3H), 7.41-7.45 (m, 2H), 7.52-7.58 (m, 4H); ^{13}C NMR (100 MHz,

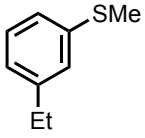


$CDCl_3$) δ 16.1, 127.1, 127.2, 127.4, 127.7, 129.1, 137.8, 138.3, 140.8; IR (KBr, ν / cm^{-1}) 1541, 1475, 823, 754.

***N,N*-Dimethyl-3-(methylthio)aniline (1h).**

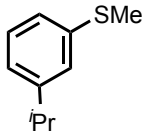
Yield: 86%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (s, 3H), 2.95 (s, 6H), 6.53-6.55 (m, 1H), 6.63-6.65 (m, 2H), 7.15-7.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 40.8, 110.0, 111.0, 114.9, 129.6, 139.2, 151.0; IR (KBr, ν / cm^{-1}) 2918, 1588, 1490, 1349, 1104, 989, 760, 685.

(3-Ethylphenyl)(methyl)sulfane (1k).



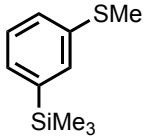
Yield: 78%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J = 7.6 Hz, 3H), 2.53 (s, 3H), 2.66 (q, J = 7.6 Hz, 2H), 7.01-7.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 15.8, 28.8, 123.8, 124.7, 126.2, 128.8, 138.1, 144.9; IR (KBr, ν / cm^{-1}) 2965, 1591, 1456, 1086, 781, 694.

(3-Isopropylphenyl)(methyl)sulfane (1l).



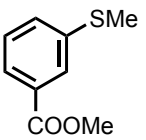
Yield: 83%;colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (d, J = 7.0 Hz, 6H), 2.52 (s, 3H), 2.91 (sep, J = 7.0 Hz, 1H), 7.04-7.27 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1, 24.1, 34.3, 123.6, 124.2, 125.2, 129.1, 138.3, 149.8; IR (KBr, ν / cm^{-1}) 2960, 1590, 1472, 1088, 967, 781, 698.

Trimethyl(3-(methylthio)phenyl)silane (1m).



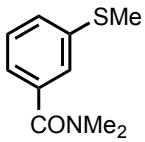
Yield: 67%; colorless oil; ^{1}H NMR (400 MHz, acetone-d_6) δ 0.26 (s, 9H), 2.49 (s, 3H), 7.28-7.30 (m, 3H), 7.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.9, 16.2, 127.2, 128.5, 130.3, 131.9, 137.9, 141.5; IR (KBr, ν / cm^{-1}) 2955, 1556, 1377, 1247, 1134, 967, 837, 751, 644.

Methyl 3-(methylthio)benzoate (1p).



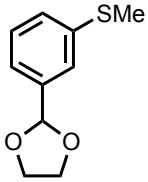
Yield: 76%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 3H), 3.92 (s, 3H), 7.33-7.36 (dd, J = 7.8, 6.9 Hz, 1H), 7.42 (d, J = 6.9 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 52.5, 126.3, 127.2, 128.9, 131.0, 139.5, 166.9; IR (KBr, ν / cm^{-1}) 2950, 1724, 1573, 1435, 1264, 1127, 968, 746, 679.

***N,N*-Dimethyl-3-(methylthio)benzamide (1q).**



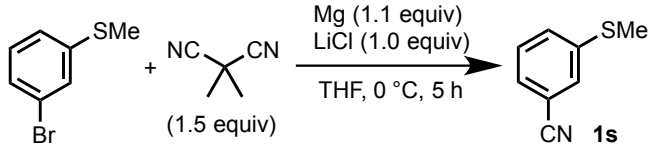
Yield: 65%; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 2.95 (s, 3H), 3.08 (s, 3H), 7.11-7.13 (m, 1H), 7.24-7.30 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 35.5, 39.8, 123.6, 124.8, 127.6, 128.9, 137.2, 139.4, 171.3; IR (KBr, ν / cm^{-1}) 3480, 2921, 1634, 1263, 1086, 935, 803, 744, 677.

2-(3-(Methylthio)phenyl)-1,3-dioxolane (1r).



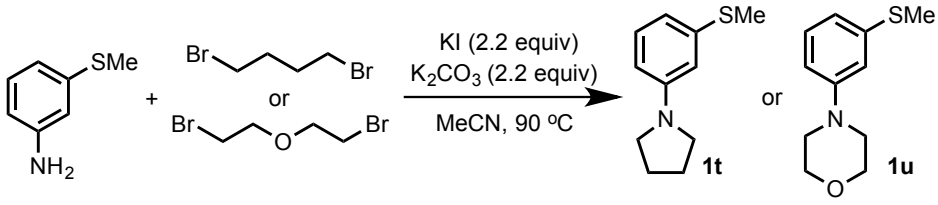
Yield: 86%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (s, 3H), 4.01-4.14 (m, 4H), 5.79 (s, 1H), 7.25-7.30 (m, 3H), 7.38 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 65.1, 103.6, 123.4, 124.6, 127.5, 129.0, 138.9, 139.0; IR (KBr, ν / cm^{-1}) 2884, 1576, 1474, 1430, 1217, 1086, 943, 787, 700.

Preparation of 3-(methylthio)benzonitrile (1s).



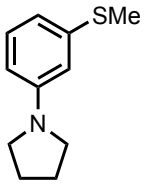
An argon-flushed round-bottomed flask was charged with anhydrous LiCl (0.630 g, 14.8 mmol) and a magnetic stir bar. The flask was dried by heating under reduced pressure and cooled to room temperature. Mg turnings (0.400 g, 16.3 mmol) and THF (5 mL) were added to the flask. To the resulting slurry, 2.5 mL solution of aryl bromide (15.0 mmol in 4.0 mL of THF) was added and the mixture was stirred vigorously. After 2-3 min, the remaining aryl bromide solution was added and stirred at room temperature for 0.5 h. To the resulting mixture, a solution of dimethylmalononitrile (2.08 g, 22.2 mmol in 15 mL THF) was added at 0 ^{o}C and the reaction mixture was allowed to warm up to room temperature for 3 h. The reaction mixture was extracted with Et_2O (20 mL). The organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuum. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 5/1) to provide benzonitrile **1s**. Yield: 65%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (s, 3H), 7.34-7.44 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 113.2, 118.7, 128.4, 128.9, 129.5, 130.5, 141.1; IR (KBr, ν / cm^{-1}) 2922, 2229, 1566, 1473, 1197, 1100, 844, 787, 680.

Preparation of 3-heterocycle substituted thiolanisole (1t and **1u)**



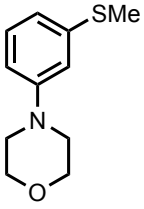
A mixture of 3-(methylthio)aniline (5.00 g, 36.0 mmol), 1,4-dibromobutane (5.90 g, 27.7 mmol) or bis(2-bromoethyl)ether (10.0 g, 43.2 mmol), potassium iodide (10.1 g, 60.9 mmol), and potassium carbonate (8.40 g, 60.9 mmol) in acetonitrile (100 mL) was heated at 90 ^{o}C for 12 h. Then the reaction mixture was cooled to room temperature and filtered. The filtrate was concentrated in vacuo and purified by a flash chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to afford an oily product.

1-(3-(Methylthio)phenyl)pyrrolidine (1t).



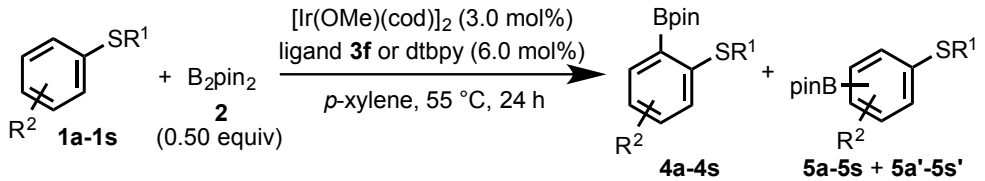
Yield: 75%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.97-2.02 (m, 4H), 2.48 (s, 3H), 3.26-3.29 (m, 4H), 6.35 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.47-6.48 (m, 1H), 6.56 (d, *J* = 7.8 Hz, 1H), 7.12 (ddd, *J* = 8.2, 8.2, 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 25.7, 47.8, 109.2, 110.1, 113.9, 129.7, 139.1, 148.4; IR (KBr, ν / cm^{-1}) 2966, 1588, 1101, 960, 822, 757, 684.

4-(3-(Methylthio)phenyl)morpholine (1u).



Yield: 80%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54 (s, 3H), 3.20 (t, *J* = 5.0 Hz, 4H), 3.90 (t, *J* = 5.0 Hz, 4H), 6.75 (dd, *J* = 8.2 Hz, 2.3 Hz, 1H), 6.83-6.88 (m, 2H), 7.24 (t, *J* = 8.2 Hz, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 49.4, 67.1, 113.0, 114.2, 118.2, 129.8, 139.6, 151.8; IR (KBr, ν / cm^{-1}) 2853, 1587, 1484, 1235, 1121, 989, 769, 687.

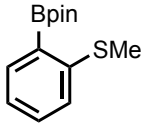
General procedure for *ortho*-selective C-H borylation of aryl sulfides 1a-s.



Aryl sulfide (**1**, 0.500 mmol), B_2pin_2 (**2**, 63.5 mg, 0.250 mmol, 0.50 equiv),

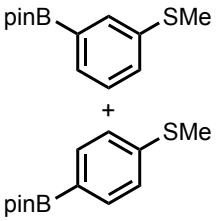
[Ir(OMe)(cod)]$_2$ (9.94 mg, 0.0150 mmol, 3.0 mol%), ligand **3f** (11.1 mg, 0.0300 mmol, 6.0 mol%), and *p*-xylene (1.5 mL) were added into a 10 mL sealed tube. The mixture was stirred at 55 ^{o}C for 24 h. Then, the solvent was removed under vacuum, and borylation products **4**, **5**, and **5′** were separated by column chromatography on silica gel (hexane/EtOAc = 10/1).

4,4,5,5-Tetramethyl-2-(2-(methylthio)phenyl)-1,3,2-dioxaborolane (4a).



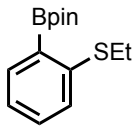
Ligand **3f**: The mixture of product (86 mg, 69% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4a** was obtained by further purification of the crude mixture by GPC (78 mg, 63% yield), white solid (mp 70-73 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.45 (s, 3H), 7.08-7.11 (m, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.35-7.39 (m, 1H), 7.68 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 25.0, 84.2, 123.8, 124.0, 131.5, 136.1, 145.4; IR (KBr, ν / cm^{-1}) 2976, 1591, 1352, 963, 863, 791, 702, 667; HRMS (ESI^{+}) Calcd for $C_{13}H_{19}BO_2SNa$ ([M+Na]$^{+}$ 273.1091, Found 273.1104.

2-Methylthio-phenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5a+5a′).



dtbpy: The mixture of product (88 mg, 70% yield, *ortho*/*meta* + *para* = 0.22); *meta*- and *para*- (**5a+5a′**) was obtained by further purification of the mixture by GPC (58 mg, 46% yield), colorless oil; *meta*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 12H), 2.46 (s, 3H), 7.24-7.28 (m, 1H), 7.31 (d, *J* = 6.9 Hz, 1H), 7.54 (d, *J* = 7.3 Hz, 1H), 7.68 (s, 1H); *para*-isomer: δ 1.38 (s, 12H), 2.53 (s, 3H), 7.26-7.28 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *meta*-isomer: δ 16.0, 25.0, 84.1, 128.4, 129.7, 131.6, 132.9, 138.0; *para*-isomer: δ 15.2, 25.1, 83.9, 125.2, 135.3, 142.8; IR (KBr, ν / cm^{-1}) 2974, 1583, 1348, 1048, 959, 857, 738, 654, 751, 644. HRMS (ESI^{+}) Calcd for $C_{13}H_{19}BO_2SNa$ ([M+Na]$^{+}$ 273.1091, Found 273.1098.

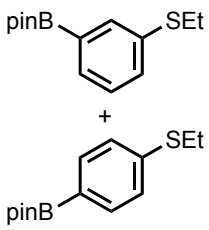
2-(2-(Ethylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4b).



Ligand **3f**: The mixture of product (95 mg, 72% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4b** was obtained by further purification of the crude mixture by GPC (89 mg, 67% yield), white solid (mp. 48-50 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.8 Hz, 3H), 1.36 (s, 12H), 2.92 (q, *J* = 7.8

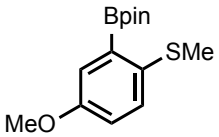
Hz, 2H), 7.09-7.13 (m, 1H), 7.24 (d, J = 7.8 Hz, 1H), 7.29 (d, J = 7.3 Hz, 1H), 7.61 (d, J = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 25.1, 27.7, 84.2, 124.7, 127.1, 131.1, 135.7, 143.3; IR (KBr, ν / cm^{-1}) 2974, 1584, 1344, 1141, 1047, 960, 856, 739, 655; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_2SNa$ ($[M+Na]^+$ 287.1248, Found 287.1248.

2-Ethylthio-phenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5b+5b′).



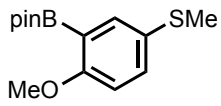
dtbpy: The mixture of product (110 mg, 83% yield, *ortho*/*meta* + *para* = 0.29); *meta*- and *para*- isomers (**5b+5b′**) were obtained by further purification of the crude mixture by GPC (77 mg, 58% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) *meta*-isomer: δ 1.28 (t, J = 7.4 Hz, 3H), 1.31 (s, 12H), 2.94 (q, J = 7.4 Hz, 2H), 7.23-7.28 (m, 2H), 7.57 (d, J = 7.3 Hz, 1H), 7.75 (s, 1H); *para*-isomer: δ 1.28-1.34 (s, 15H), 2.95 (q, J = 7.3 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *meta*-isomer: δ 14.6, 25.1, 27.9, 84.1, 128.4, 132.1, 132.3, 135.6, 136.3; *para*-isomer: δ 14.2, 24.9, 26.5, 83.8, 126.8, 135.2, 141.2; IR (KBr, ν / cm^{-1}) 2977, 1596, 1359, 1144, 1103, 1016, 962, 859, 729, 653; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_2SNa$ ($[M+Na]^+$ 287.1248, Found 287.1256.

2-(5-Methoxy-2-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4c).



Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (92 mg, 66% yield, *ortho*/*meta* + *para* = >20); *ortho*-borylated product **4c** was obtained by further purification by GPC (70 mg, 50% yield), white solid (mp. 71-73 ^{o}C); ^{1}H NMR (400 MHz, acetone-d_6) δ 1.35 (s, 12H), 2.39 (s, 3H), 3.78 (s, 3H), 6.98 (dd, J = 8.7, 3.2 Hz, 1H), 7.14 (d, J = 3.2 Hz, 1H), 7.26 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 25.1, 55.6, 84.3, 117.5, 120.6, 128.5, 135.2, 157.3; IR (KBr, ν / cm^{-1}) 2972, 1561, 1349, 1152, 1056, 964, 863, 703; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_3S$ ([M]) 280.1304, Found 280.1300.

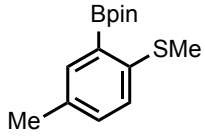
4,4,5,5-Tetramethyl-2-(2-methyl-5-(methylthio)phenyl)-1,3,2-dioxaborolane (5c).



dtbpy: A mixture of *ortho*- and *meta*-borylated products (88 mg, 63% yield, *ortho*/*meta* + *para* = 1.0); yellow solid; ^{1}H NMR (400 MHz, acetone-d_6) δ 1.33 (s, 12H), 2.42 (s, 3H), 3.78 (s, 3H), 6.95 (d, J = 8.7 Hz, 1H), 7.41 (d, J = 8.7 Hz, 1H), 7.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.5, 25.0,

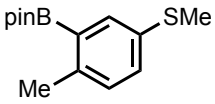
56.3, 83.9, 111.5, 128.4, 133.5, 137.8, 163.1; IR (KBr, ν / cm^{-1}) 2967, 1564, 1351, 1150, 1057, 964, 864, 828, 703; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_3SH$ ($[M+H]^+$) 303.1197, Found 303.1200.

4,4,5,5-Tetramethyl-2-(5-methyl-2-(methylthio)phenyl)-1,3,2-dioxaborolane (4d).



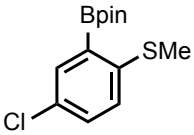
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (96 mg, 73% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4d** was obtained by further purification by GPC (74 mg, 56% yield), white solid (mp. 85-87 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.29 (s, 3H), 2.43 (s, 3H), 7.08 (d, *J* = 7.8, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.51 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 20.9, 25.1, 84.1, 124.8, 132.2, 133.5, 136.8, 141.7; IR (KBr, ν / cm^{-1}) 2980, 1339, 1144, 1068, 964, 873, 730; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_2S$ ($[M]^+$) 264.1355, Found 264.1343.

4,4,5,5-Tetramethyl-2-(2-methyl-5-(methylthio)phenyl)-1,3,2-dioxaborolane (5d).



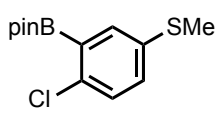
dtbpy: A mixture of *ortho*- and *meta*-borylated products (79 mg, 61% yield, *ortho*/*meta* + *para* = 2.0); *meta*-Isomer **5d** was obtained by further purification by GPC (18 mg, 14% yield), yellow solid (mp. 85-87 °C); ^1H NMR (400 MHz, acetone-d_6) δ 1.35 (s, 12H), 2.46 (s, 6H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 1H), 7.63 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.9, 21.9, 25.1, 83.8, 130.1, 130.7, 134.2, 135.1, 142.3; IR (KBr, ν / cm^{-1}) 2980, 1590, 1337, 1144, 964, 873, 730; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_2S$ ($[M]^+$) 264.1355, Found 264.1343.

2-(5-Chloro-2-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4e).



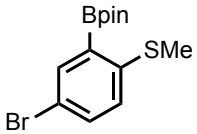
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (114 mg, 80% yield, *ortho*/*meta* + *para* = 12); *ortho*-borylated product **4e** was obtained by further purification by GPC (70 mg, 49% yield), white solid (mp. 80-82 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 2.43 (s, 3H), 7.08 (d, *J* = 8.7 Hz, 1H), 7.32 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.64 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ16.2, 25.1, 84.6, 125.6, 130.1, 131.3, 135.8, 143.9; IR (KBr, ν / cm^{-1}) 2978, 1392, 1334, 1244, 1141, 1106, 1042, 862. HRMS (ESI^+) Calcd for $C_{13}H_{18}BClO_2SNa$ ($[M+Na]^+$) 307.0701, Found 307.0687.

2-(2-Chloro-5-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5e).



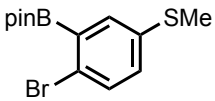
dtbpy: A mixture of *ortho*- and *meta*-borylated products (102 mg, 71% yield, *ortho*/*meta* + *para* = 2.0); white solid; ^{1}H NMR (400 MHz, acetone-d_6) δ 1.36 (s, 12H), 2.50 (s, 3H), 7.28-7.33 (m, 2H), 7.49-7.52 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 25.0, 84.5, 129.9,130.3, 134.8, 136.4, 136.6; IR (KBr, ν / cm^{-1}) 2980, 1392, 1335, 1244, 1141, 1105, 963, 862. HRMS (ESI^+) Calcd for $C_{13}H_{18}BClO_2SNa$ ($[M+Na]^+$) 307.0701, Found 307.0707.

2-(5-Bromo-2-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4f).



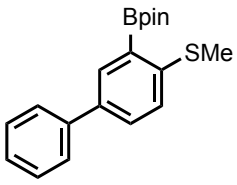
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (139 mg, 85% yield, *ortho*/*meta* + *para* = 6.6); *ortho*-borylated product **4f** was obtained by further purification by GPC (101 mg, 62% yield), yellow solid (mp. 88-90 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.43 (s, 3H), 7.00 (d, *J* = 8.7 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 25.1, 84.6, 118.0, 125.8, 134.2, 138.6, 144.7; IR (KBr, ν / cm^{-1}) 2977, 1544, 1339, 1140, 961, 868, 698. HRMS (ESI^+) Calcd for $C_{13}H_{18}BBrO_2SNa$ ($[M+Na]^+$) 351.0196, Found 351.0208.

2-(2-Bromo-5-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5f).



dtbpy: A mixture of *ortho*- and *meta*-borylated products (125 mg, 76% yield, *ortho*/*meta* + *para* = 3.0); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.49 (s, 3H), 7.11 (d, *J* = 8.2 Hz, 1H), 7.43-7.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 25.0, 84.7, 124.5, 130.2, 133.2, 134.7, 137.2; IR (KBr, ν / cm^{-1}) 2977, 1570, 1141, 1045, 962, 858, 699. HRMS (ESI^+) Calcd for $C_{13}H_{18}BBrO_2SNa$ ($[M+Na]^+$) 351.0196, Found 351.0208.

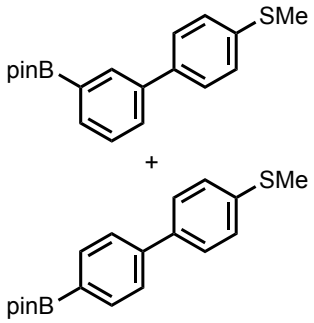
4,4,5,5-Tetramethyl-2-(4-(methylthio)biphenyl-3-yl)-1,3,2-dioxaborolane (4g).



Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (140 mg, 86% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4g** was obtained by further purification by GPC (128 mg, 79% yield), white solid (mp. 116-118 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (s, 12H), 2.51 (s, 3H), 7.26-7.28 (m, 2H), 7.33-7.35 (m, 2H), 7.61 (m, 3H), 7.95-7.96 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 25.1, 84.3, 124.5, 127.1, 127.2, 128.9, 130.0, 134.9, 136.7, 140.8, 144.7.

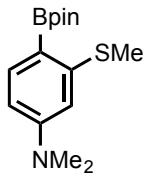
HRMS (ESI$^+$) Calcd for $C_{19}H_{23}BO_2S$ ([M]$^+$) 326.1512, Found 326.1461.

4,4,5,5-Tetramethyl-2-(4'-(methylthio)biphenyl)-1,3,2-dioxaborolane (5g+5g′).



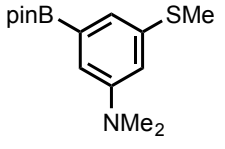
dtbpy: A mixture of *meta*- and *para*-borylated products (135 mg, 83% yield, *meta*/*para* = 1.9); *meta*- and *para*-Isomers (**5g+5g′**) were obtained by further purification by GPC (119 mg, 73% yield), white solid (mp. 112-114 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) *meta*-isomer: δ 1.36 (s, 12H), 2.52 (s, 1H), 7.31 (d, *J* = 8.7 Hz, 2H), 7.42-7.48 (m, 1H), 7.56 (d, *J* = 8.7 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 8.03 (s, 1H); para-isomer: δ 1.37 (s, 12H), 2.52 (s, 3H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 2H), 7.87 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *meta*-isomer: δ 16.2, 25.1, 84.1, 127.1, 127.8, 128.5, 129.9, 133.4, 133.8, 137.6, 138.2, 140.1; *para*-isomer: δ 16.1, 25.1, 84.1, 126.3, 127.1, 127.8, 135.5, 138.0, 138.3, 143.4; IR (KBr, ν / cm^{-1}) 2973, 1420, 1358, 1319, 1144, 963, 864, 798, 709; HRMS (ESI$^+$) Calcd for $C_{19}H_{23}BO_2S$ ([M]$^+$) 326.1512, Found 326.1460.

***N*,*N*-Dimethyl-3-(methylthio)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (4h).**



Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (111 mg, 76% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4h** was obtained by further purification by GPC (100 mg, 68% yield), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.45 (s, 3H), 2.97 (s, 6H), 6.40-6.45 (m, 2H), 7.61 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 25.0, 40.3, 83.4, 107.5, 107.8, 138.2, 147.0, 152.7; IR (KBr, ν / cm^{-1}) 3391, 2977, 1590, 1476, 1348, 1143, 982, 851, 762, 673; HRMS (ESI$^+$) Calcd for $C_{15}H_{24}BNO_2SH$ ([M+H]$^+$) 294.1694, Found 294.1708.

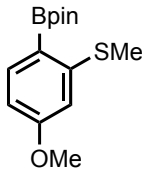
***N*,*N*-Dimethyl-3-(methylthio)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (5h).**



dtbpy: A mixture of *ortho*- and *meta*-borylated products (92 mg, 63% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer (**5h**) were obtained by

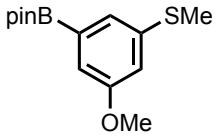
further purification by GPC (88 mg, 60% yield), yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 2.50 (s, 3H), 2.96 (s, 6H), 6.74 (s, 1H), 6.97 (s, 1H), 7.07 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 25.1, 40.9, 84.0, 114.2, 116.2, 121.3, 138.7, 150.6; IR (KBr, ν / cm^{-1}) 3391, 2977, 1590, 1478, 1349, 1143, 851,673; HRMS (ESI^+) Calcd for $C_{15}H_{24}BNO_2SH$ ($[M+H]^+$) 294.1694, Found 294.1684.

2-(4-Methoxy-2-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4i).



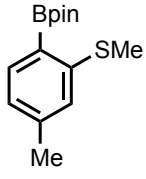
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (84 mg, 60% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4i** was obtained by further purification by GPC (71 mg, 51% yield), colorless oil; (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.43 (s, 3H), 3.83 (s, 3H), 6.61 (d, *J* = 8.2 Hz, 1H), 6.68 (s, 1H), 7.67 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 25.1, 55.4, 83.9, 108.2, 110.5, 138.4, 147.9, 162.4; IR (KBr, ν / cm^{-1}) 2976, 1563, 1351, 1235, 1151, 1056, 964, 863, 703; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_3SNa$ ($[M+Na]^+$) 303.1197, Found 303.1197.

2-(3-Methoxy-5-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5i).



dtbpy: A mixture of *ortho*- and *meta*-borylated products (97 mg, 69% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5i** were obtained by further purification by GPC (92 mg, 66% yield), white solid (mp. 73-75 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.49 (s, 3H), 3.82 (s, 3H), 6.88 (s, 1H), 7.08 (s, 1H), 7.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 25.1, 55.6, 84.2, 115.6, 116.0, 125.4, 139.6, 159.6; IR (KBr, ν / cm^{-1}) 2976, 1563, 1351, 1235, 1151, 1056, 964, 863, 703; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_3SNa$ ($[M+Na]^+$) 303.1197, Found 303.1196.

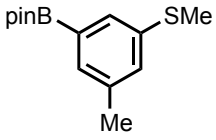
4,4,5,5-Tetramethyl-2-(4-methyl-2-(methylthio)phenyl)-1,3,2-dioxaborolane (4j).



Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (85 mg, 64% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4j** was obtained by further purification by GPC (76 mg, 58% yield), yellow solid (mp. 58-60 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 2.34 (s, 3H), 2.44 (s, 3H), 6.90 (d, *J* = 7.8 Hz, 1H), 6.96 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 22.0, 25.0, 84.0, 124.6, 124.7, 136.4, 141.6, 145.4; IR (KBr, ν / cm^{-1}) 2968,

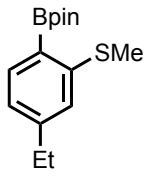
1572, 1354, 1214, 1152, 964, 863, 706; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_2S$ ($[M]^+$) 264.1355, Found 264.1344.

4,4,5,5-Tetramethyl-2-(3-methyl-5-(methylthio)phenyl)-1,3,2-dioxaborolane (5j).



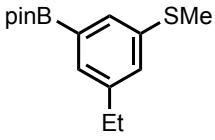
dtbpy: A mixture of *ortho*- and *meta*-borylated products (82 mg, 62% yield, *ortho*/*meta* + *para* = 0.16); *meta*-Isomer **5j** was obtained by further purification by GPC (65 mg, 48% yield), white solid; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 2.32 (s, 3H), 2.44 (s, 3H), 7.18 (s, 1H), 7.39 (s, 1H), 7.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1, 21.4, 25.1, 84.1, 130.1, 130.5, 132.5, 137.9, 138.1; IR (KBr, ν / cm^{-1}) 2968, 1354, 1214, 1152, 863, 706; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_2S$ ($[M]^+$) 264.1355, Found 264.1344.

2-(4-Ethyl-2-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4k).



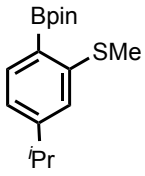
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (122 mg, 88% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4k** was obtained by further purification by GPC (111 mg, 80% yield), colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, 3H), 1.34 (s, 12H), 2.44 (s, 3H), 2.60 (q, *J* = 7.8 Hz, 2H), 6.93 (d, *J* = 7.3 Hz, 1H), 6.99 (s, 1H), 7.62 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 15.9, 25.1, 29.4, 84.0, 123.6, 123.7, 136.6, 145.4, 148.0; IR (KBr, ν / cm^{-1}) 2975, 1595, 1348, 1145, 1108, 1046, 852, 662; HRMS (ESI^+) Calcd for $C_{15}H_{23}BO_2SH$ ($[M+H]^+$) 279.1585, Found 279.1585.

2-(3-Ethyl-5-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5k).



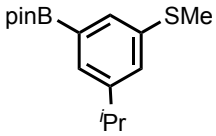
Yield: A mixture of *ortho*- and *meta*-borylated products (103 mg, 74% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5k** was obtained by further purification by GPC (93 mg, 67% yield), colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, *J* = 6.9 Hz, 6.8 Hz, 3H), 1.34 (s, 12H), 2.50 (s, 3H), 2.59 (q, *J* = 6.9 Hz, 2H), 7.20 (s, 1H), 7.42 (s, 1H), 7.52 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 16.2, 25.0, 29.0, 84.1, 129.5, 130.4, 131.5, 137.9, 144.5; IR (KBr, ν / cm^{-1}) 2975, 1596, 1349, 1269, 1145, 1109, 1046, 962, 852, 642; HRMS (ESI^+) Calcd for $C_{15}H_{23}BO_2SH$ ($[M+H]^+$) 279.1585, Found 279.1585.

2-(4-Isopropyl-2-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4l).



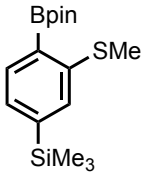
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (91 mg, 62% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4l** was obtained by further purification by GPC (80 mg, 54% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (d, *J* = 7.3 Hz, 6H), 1.36 (s, 12H), 2.46 (s, 3H), 2.89 (sep, *J* = 7.3 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 7.02 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 24.0, 25.1, 34.7, 84.0, 112.1, 122.6, 136.6, 145.3, 152.6; IR (KBr, ν / cm^{-1}) 2975, 1594, 1545, 1352, 1142, 1045, 962, 861, 666; HRMS (ESI^+) Calcd for $C_{16}H_{25}BO_2SNa$ ($[M+Na]^+$) 315.1561, Found 315.1568.

2-(3-Isopropyl-5-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5l).



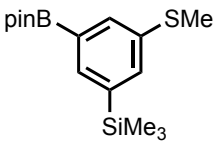
dtbpy: A mixture of *ortho*- and *meta*-borylated products (92 mg, 63% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5l** was obtained by further purification by GPC (86 mg, 59% yield), white solid (mp. 60-62 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (d, *J* = 6.9 Hz, 6H), 1.34 (s, 12H), 2.49 (s, 3H), 2.89 (sep, *J* = 6.9 Hz, 1H), 7.23-7.24 (s, 1H), 7.43 (s, 1H), 7.52 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 24.2, 25.1, 34.4, 84.1, 128.2, 130.1, 130.5, 137.9, 149.0; IR (KBr, ν / cm^{-1}) 2975, 1594, 1351, 1142, 861, 666; HRMS (ESI^+) Calcd for $C_{16}H_{25}BO_2SNa$ ($[M+Na]^+$) 315.1561, Found 315.1568.

Trimethyl(3-(methylthio)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)silane (4m).



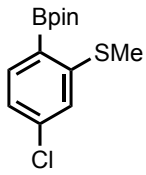
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (134 mg, 83% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4m** was obtained by further purification by GPC (120 mg, 74% yield), yellow solid (mp. 98-100 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.27 (s, 9H), 1.36 (s, 12H), 2.48 (s, 3H), 7.25-7.27 (m, 1H), 7.32 (s, 1H), 7.65 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -1.1, 16.2, 25.0, 84.2, 128.9, 129.1, 135.2, 144.2, 144.4; IR (KBr, ν / cm^{-1}) 2978, 1580, 1344, 1249, 1137, 964, 857, 754, 707; HRMS (ESI^+)Calcdfor $C_{16}H_{27}BO_2SSi$ Na ($[M+Na]^+$) 345.1486, Found 345.1492.

Trimethyl(3-(methylthio)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)silane (5m).



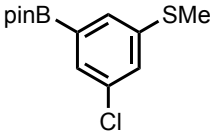
dtbpy: A mixture of *ortho*- and *meta*-borylated products (126 mg, 78% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5m** was obtained by further purification by GPC (114 mg, 71% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.28 (s, 9H), 1.35 (s, 12H), 2.52 (s, 3H), 7.51 (s, 1H), 7.70 (s, 1H), 7.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.8, 16.3, 25.1, 84.1, 133.6, 134.9, 136.6, 137.3, 140.6; IR (KBr, ν / cm^{-1}) 2978, 1344, 1249, 1137, 964, 856, 754, 707, 751; HRMS (ESI^+) Calcdfor $C_{16}H_{27}BO_2SSiNa$ ($[M+Na]^+$) 345.1486, Found 345.1491.

2-(4-Chloro-2-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4n).



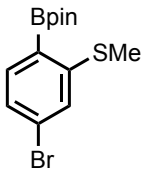
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (91 mg, 64% yield, *ortho*/*meta* + *para* = 5.1); *ortho*-borylated product **4n** was obtained by further purification by GPC (60 mg, 42% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 2.43 (s, 3H), 7.02-7.06 (m, 2H), 7.59-7.61 (m, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 25.0, 84.3, 123.3, 123.8, 137.5, 137.9, 148.0; IR (KBr, ν / cm^{-1}) 2978, 1576, 1342, 1145, 1105, 1046, 962, 831, 650. HRMS (ESI^+) Calcdfor $C_{13}H_{18}BClO_2SNa$ ($[M+Na]^+$) 307.0701, Found 307.0699.

2-(3-Chloro-5-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5n).



dtbpy: A mixture of *ortho*- and *meta*-borylated products (107 mg, 75% yield, *ortho*/*meta* + *para* = <0.01); *meta*-iIsomer **5n** was obtained by further purification by GPC (93 mg, 66% yield), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.49 (s, 3H), 7.27-7.28 (dd, *J* = 2.3, 1.8 Hz, 1H), 7.52-7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 25.1,84.5, 128.7, 130.8, 131.2, 134.7, 140.4; IR (KBr, ν / cm^{-1}) 2978, 1555, 1342, 1144, 964, 873, 794, 701. HRMS (ESI^+) Calcdfor $C_{13}H_{18}BClO_2SNa$ ($[M+Na]^+$) 307.0701, Found 307.0695.

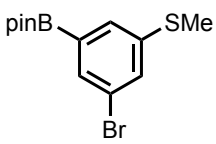
2-(4-Bromo-2-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4o).



Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (130 mg, 79% yield, *ortho*/*meta* + *para* = 6.7); *ortho*-borylated product **4o** was obtained by further purification by GPC (96 mg, 59% yield), colorless oil; ^{1}H NMR (400

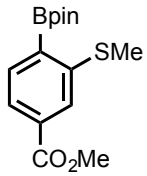
MHz, $CDCl_3$) δ 1.38 (s, 12H), 2.47 (s, 3H), 7.23-7.28 (m, 2H), 7.56 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 25.1,84.4, 126.2, 126.6, 126.8, 137.6, 148.1; IR (KBr, ν / cm^{-1}) 2977, 1569, 1341, 1145, 1045, 858. HRMS (ESI^+) Calcd for $C_{13}H_{18}BBrO_2SNa$ ([M+Na]$^+$) 351.0196, Found 351.0185.

2-(3-Bromo-5-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5o).



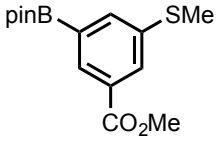
dtbpy: A mixture of *ortho*- and *meta*-borylated products (118 mg, 72% yield, *ortho*/*meta* + *para* = 0.13); *meta*-Isomer **5o** was obtained by further purification of the crude mixture by GPC (86 mg, 52% yield), yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 12H), 2.48 (s, 3H), 7.43 (s, 1H), 7.58 (s, 1H), 7.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 25.0, 84.5, 123.0, 131.2, 131.4, 134.0, 140.7; IR (KBr, ν / cm^{-1}) 2978, 1546, 1341, 1213, 1144, 963, 869, 769, 700. RMS (ESI^+) Calcd for $C_{13}H_{18}BBrO_2SNa$ ([M+Na]$^+$) 351.0196, Found 351.0179.

3-(Methylthio)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate ester (4p).



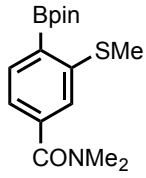
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (137 mg, 89% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4p** was obtained by further purification by GPC (130 mg, 84% yield), colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.49 (s, 3H), 3.90 (s,3H), 7.69-7.71 (m, 2H), 7.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 25.0, 52.4, 84.6, 124.4, 124.6, 132.6, 135.9, 146.1, 167.1; IR (KBr, ν / cm^{-1}) 2978, 1715, 1384, 962, 852, 731, 650; HRMS (ESI^+) Calcd for $C_{15}H_{21}BO_4SNa$ ([M+Na]$^+$) 331.1146, Found 331.1157.

3-(Methylthio)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (5p).



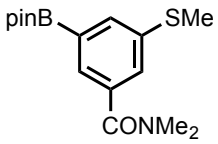
dtbpy: A mixture of *ortho*- and *meta*-borylated products (128 mg, 83% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5p** was obtained by further purification by GPC (116 mg, 75% yield), white solid (mp. 115-117 ^oC); ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.52 (s, 3H), 3.90 (s, 3H), 7.84 (s, 1H), 7.97(s, 1H), 8.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 25.1, 52.4, 84.4, 129.9, 130.4, 132.5, 137.1, 139.0, 167.0; IR (KBr, ν / cm^{-1}) 2950, 1724, 1435, 1127, 968, 846, 679; HRMS (ESI^+) Calcd for$C_{15}H_{21}BO_4SNa$ ([M+Na]$^+$) 331.1146, Found 331.1157.

_N_,_N_-Dimethyl-3-(methylthio)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (4q).



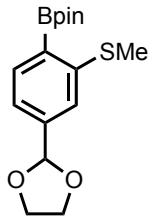
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (124 mg, 77% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4q** was obtained by further purification by GPC (91 mg, 57% yield), yellow solid (mp. 118-120 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.45 (s, 3H), 2.93 (s, 3H), 3.10 (s, 3H), 7.07 (d, *J* = 7.8 Hz, 1H), 7.17 (s, 1H), 7.69 (d, *J* = 7.8, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 25.1, 35.5, 39.7, 84.5, 122.0, 122.2, 136.0, 139.2, 146.4, 171.5; IR (KBr, ν / cm^{-1}) 3466, 2977, 1633, 1348, 1143, 965, 871, 791, 756, 706, 652; HRMS (ESI^{+}) Calcd for $C_{16}H_{24}BNO_3SNa$ ([M+Na]$^{+}$) 344.1462, Found 344.1466.

_N_,_N_-Dimethyl-3-(methylthio)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (5q).



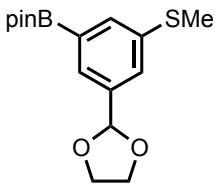
dtbpy: A mixture of *ortho*- and *meta*-borylated products (136 mg, 85% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5q** was obtained by further purification by GPC (127 mg, 79% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 12H), 2.48 (s, 3H), 2.95 (s, 3H), 3.07 (s, 3H), 7.34 (s, 1H), 7.55 (s, 1H), 7.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ15.8, 25.0, 35.4, 39.8, 84.3, 127.4, 129.6, 133.7, 136.6, 138.8, 171.4; IR (KBr, ν / cm^{-1}) 3465, 2977, 1633, 1348, 1143, 965, 871, 791, 756, 706, 652; HRMS (ESI^{+}) Calcd for $C_{16}H_{24}BNO_3SNa$ ([M+Na]$^{+}$) 344.1462, Found 344.1475.

2-(4-(1,3-Dioxolan-2-yl)-2-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4r).



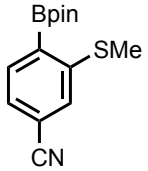
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (145 mg, 90% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4r** was obtained by further purification by GPC (132 mg, 82% yield), white solid (mp. 48-50 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 2.47 (s,3H), 4.02-4.11 (m,4H), 5.82 (s, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.26 (s, 1H), 7.67 (d, *J* = 7.8Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 25.1, 65.4, 84.3, 103.6, 121.7, 121.8, 136.3, 141.2, 145.9; IR (KBr, ν / cm^{-1}) 2977, 1598, 1355, 1143, 869, 707, 669, 644; HRMS (ESI^{+}) Calcd for $C_{16}H_{23}BO_4SNa$ ([M+Na]$^{+}$ 345.1302, Found 345.1316.

2-(3-(1,3-Dioxolan-2-yl)-5-(methylthio)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5r).



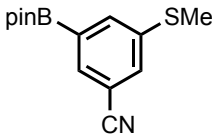
dtbpy: A mixture of *ortho*- and *meta*-borylated products (148 mg, 92% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5r** was obtained by further purification by GPC (125 mg, 78% yield), white solid (mp. 52-54 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 2.50 (s, 1H), 4.02-4.13 (m, 4H), 5.78 (s, 1H), 7.46(s, 1H), 7.68 (s, 1H), 7.69 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1, 25.1, 65.5, 84.2, 103.7, 127.5, 129.8, 133.8, 138.1, 138.5; IR (KBr, ν / cm^{-1}) 2978, 1599, 1353, 1214, 1143, 964, 869, 706; HRMS (ESI^{+}) Calcd for $C_{16}H_{23}BO_4SNa$ ([M+Na]$^{+}$ 345.1302, Found 345.1316.

3-(Methylthio)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (4s).



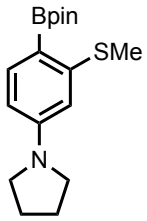
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (103 mg, 75% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4s** was obtained by further purification by GPC (74 mg, 54% yield), white solid (mp. 68-70 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.47 (s, 3H), 7.34 (s, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.73-7.75 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 25.3,84.9, 115.1, 119.0, 126.3, 126.8, 136.4, 147.6; IR (KBr, ν / cm^{-1}) 2974, 2237, 1567, 1356, 1155, 967, 860, 700; HRMS (ESI^{+}) Calcd for $C_{14}H_{18}BNO_2SNa$ ([M+Na]$^{+}$) 298.1044, Found 298.1038.

3-(Methylthio)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (5s).



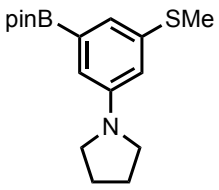
dtbpy: A mixture of *ortho*- and *meta*-borylated products (112 mg, 82% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5s** was obtained by further purification of the crude mixture by GPC (67 mg, 60% yield), white solid (mp. 75-77 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 12H), 2.48 (s, 3H), 7.49 (s, 1H), 7.79 (s, 1H), 7.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 25.0, 84.8, 112.9, 118.7, 131.1, 134.6, 136.5, 140.4; IR (KBr, ν / cm^{-1}) 2974, 2237, 1568, 1357, 1201, 1151, 967, 898, 761, 700; HRMS (ESI^{+}) Calcd for $C_{14}H_{18}BNO_2SNa$ ([M+Na]$^{+}$) 298.1044, Found 298.1046.

1-(3-(Methylthio)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pyrrolidine (4t).



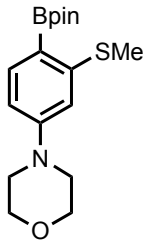
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (112 mg, 70% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4t** was obtained by further purification by GPC (99 mg, 62% yield), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 1.98 (t, *J* = 6.4 Hz, 4H), 2.44 (s, 3H), 3.30 (t, *J* = 6.4 Hz Hz, 4H), 6.27-6.29 (m, 2H), 7.59 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 25.1, 25.6, 47.6, 83.4, 107.0, 107.5, 138.3, 147.2, 150.2; IR (KBr, ν / cm^{-1}) 2968, 2359, 1588, 1487, 650; HRMS (ESI^+) Calcd for $C_{17}H_{26}BNO_2SNa$ ($[M+Na]^+$) 342.1670, Found 342.1676.

1-(3-(Methylthio)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pyrrolidine (5t).



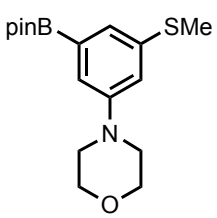
dtbpy: A mixture of *ortho*- and *meta*-borylated products (101 mg, 63% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5t** was obtained by further purification by GPC (86 mg, 54% yield), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 1.96 (t, *J* = 6.6 Hz, 4H), 2.50 (s, 3H), 3.29 (t, *J* = 6.6 Hz, 4H), 6.57 (s, 1H), 6.80 (s, 1H), 7.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 25.1, 25.7, 47.9, 83.9, 113.0, 115.4, 120.1, 138.6, 147.9; IR (KBr, ν / cm^{-1}) 2967, 2359, 1588, 1487, 1373, 756; HRMS (ESI^+) Calcd for $C_{17}H_{26}BNO_2SNa$ ($[M+H]^+$) 320.1850, Found 320.1853.

4-(3-(Methylthio)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)morpholine (4u).



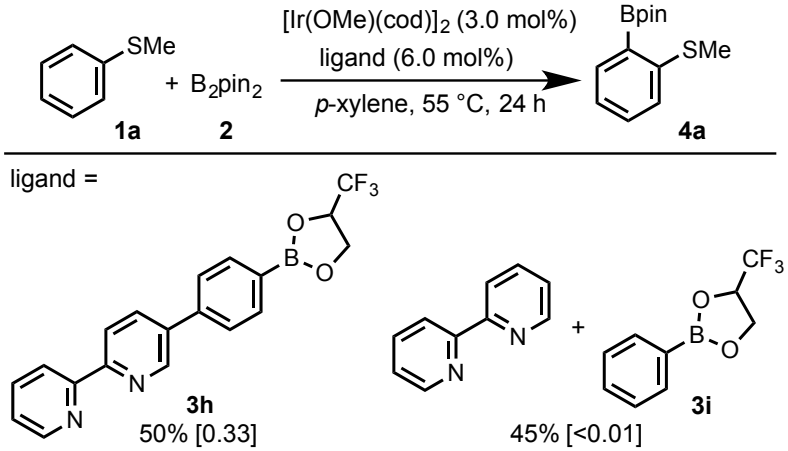
Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (122 mg, 73% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **4u** was obtained by further purification by GPC (102 mg, 61% yield), white solid (mp. 92-94 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.43 (s, 3H), 3.20 (t, *J* = 4.8 Hz, 4H), 3.83 (t, *J* = 4.8 Hz, 4H), 6.59-6.62 (m, 1H), 6.65 (s, 1H), 7.62 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 25.0, 48.6, 66.9, 83.7, 110.6, 110.7, 138.0, 147.1, 153.7; IR (KBr, ν / cm^{-1}) 2976, 1565, 1427, 1371, 1316, 1231, 1115, 989, 706; HRMS (ESI^+) Calcd for $C_{17}H_{26}BNO_3S$ Na ($[M+Na]^+$) 358.1619, Found 358.1630.

4-(3-(Methylthio)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)morpholine (5u).



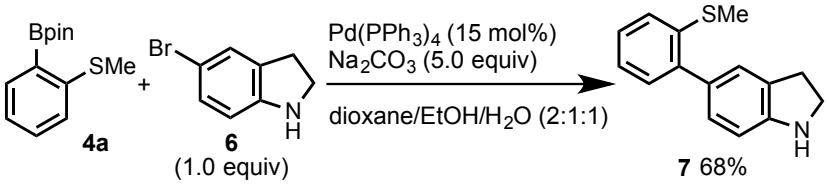
dtbpy: A mixture of *ortho*- and *meta*-borylated products (125 mg, 75% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **5u** was obtained by further purification by GPC (110 mg, 66% yield), white solid (mp. 73-75 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 2.50 (s, 3H), 3.17 (t, *J* = 5.0 Hz, 4H), 3.83 (t, *J* = 5.0 Hz, 4H), 6.90 (s, 1H), 7.14 (s, 1H), 7.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 25.1, 49.6, 67.1, 84.1, 117.3, 119.2, 124.5, 139.1, 151.2; IR (KBr, ν / cm^{-1}) 2976, 1566, 1427, 1371, 1231, 1115, 989, 854, 706; HRMS (ESI^{+}) Calcd for $C_{17}H_{26}BNO_3SNa$ ([M+Na]$^{+}$) 358.1619, Found 358.1631.

Control experiments.



In order to confirm the importance of the positions of a catalytic site and boryl group, we investigated C-H borylation reactions using ligand **3h** or a mixture of bipyridine and **3i** as a ligand. These results indicated that the Lewis acid-base interaction worked during the reaction and played an important role for the high *ortho*-selectivity.

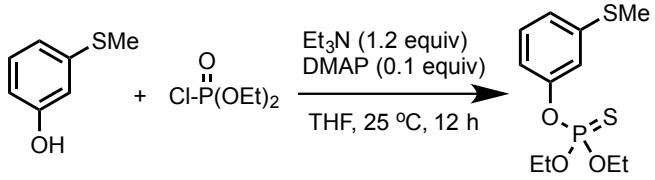
Synthesis of 5-(2-(methylthio)phenyl)indoline.



Into a 50 mL two-necked flask equipped with a reflux condenser, **4a** (100 mg, 0.400 mmol), 5-bromoindoline (**6**, 79.2 mg, 0.400 mmol), $Pd(PPh_3)_4$ (69.3 mg, 0.0600 mmol),

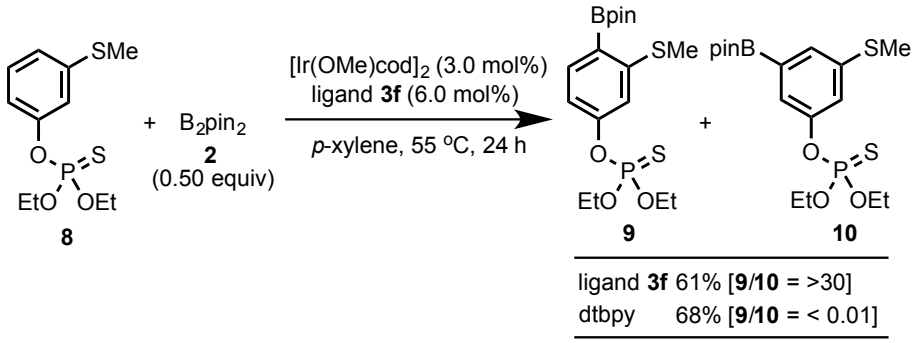
sodium carbonate (212 mg, 2.00 mmol), dioxane (10 mL), ethanol (5.0 mL), and H_2O (25 mL) were added. Then the mixture was heated at 90 ^oC for 12 h. The reaction mixture was cooled to room temperature and was extracted with EtOAc (2 x 15 mL). Then the organic phase was washed with H_2O and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed under vacuum to give a yellow oil crude product, which was purified by GPC to give **7** as a brown oil. Yield: (65.6 mg, 68%); ^1H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 3.14 (t, J = 8.5 Hz, 2H), 3.66 (t, J = 8.5 Hz, 2H), 6.77 (d, J = 8.3 Hz, 1H), 7.15 (d, J = 8.2 Hz, 1H), 7.24-7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 29.7, 47.4, 108.8, 124.4, 124.6, 125.6, 127.2, 128.4, 129.2, 129.9, 131.0, 137.2, 141.3, 150.8.

Preparation of *O*,*O*-diethyl *O*-(3-(methylthio)phenyl) phosphorothioate (8).



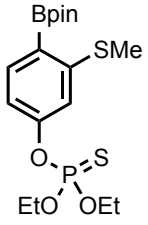
A mixture of 3-(methylthio)phenol (1.30 g, 8.90 mmol), Et_3N (1.20 g, 10.6 mmol), and DMAP (0.120 g, 0.900 mmol) in THF (15 mL) was stirred at 25 ^oC for 1 h, and then diethyl phosphorochloridate was added dropwise into the mixture. After 12 h, the reaction mixture was extracted with ethyl ether and the organic layer was concentrated in vacuo. The crude product was purified by chromatography on silica gel (hexane/ethyl acetate = 10/1) to give an oily product. Yield: 85%; colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, J = 7.1 Hz, 6H), 2.49 (s, 3H), 4.21-4.30 (m, 4H), 6.97 (dd, J = 8.2, 3.3 Hz, 1H), 7.09 (d, J = 1.4 Hz, 1H), 7.23-7.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 15.9 (d, J = 7.6 Hz), 65.1 (d, J = 5.7 Hz), 117.3 (d, J = 3.8 Hz), 118.6 (d, J = 4.8 Hz), 123.1 (d, J = 1.9 Hz), 129.6, 140.3, 151.0 (d, J = 7.6 Hz); IR (KBr, ν / cm^{-1}) 2983, 1590, 1473, 1265, 1208, 1024, 824, 680.

C-H borylation of a bioactive compound.



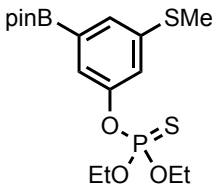
O,*O*-Diethyl *O*-3-(methylthio)phenyl phosphorothioate (**8**, 146 mg, 0.500 mmol), B_2pin_2 (**2**, 63.5 mg, 0.250 mmol, 0.50 equiv), $[Ir(OMe)cod]_2$ (9.94 mg, 0.0150 mmol, 3.0 mol%), ligand **3f** (11.1 mg, 0.0300 mmol, 6.0 mol%), and *p*-xylene (1.5 mL) were added into a 10 mL sealed tube. Then the mixture was stirred at 55 °C for 24 h, and the solvent was removed under vacuum. Borylation products **9** and **10** were isolated by column chromatography on silica gel (hexane/EtOAc = 10/1).

***O*,*O*-Diethyl-*O*-3-(methylthio)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl Phosphorothioate (9).**



Ligand **3f**: A mixture of *ortho*- and *meta*-borylated products (123 mg, 61% yield, *ortho*/*meta* + *para* = >30); *ortho*-borylated product **9** was obtained by further purification by GPC (110 mg, 55% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33-1.36 (m, 18H), 2.43 (s, 3H), 4.18-4.26 (m, 4H), 6.89 (d, *J* = 8.2 Hz, 1H), 6.99 (s, 1H), 7.67 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 16.1, 16.2, 25.1, 65.3, 65.4, 84.3, 115.9 (d, *J* = 4.8 Hz), 116.2 (d, *J* = 5.7 Hz), 137.8, 148.1 , 153.4 (d, *J* = 7.4 Hz); IR (KBr, ν / cm^{-1}) 2979, 1567, 1349, 1024, 826, 702; HRMS (ESI^+) Calcd for $C_{17}H_{28}BO_5PS_2Na$ ($[M+Na]^+$) 441.1101, Found 441.1095.

***O*,*O*-Diethyl-*O*-3-(methylthio)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenylphosphorothioate (10).**

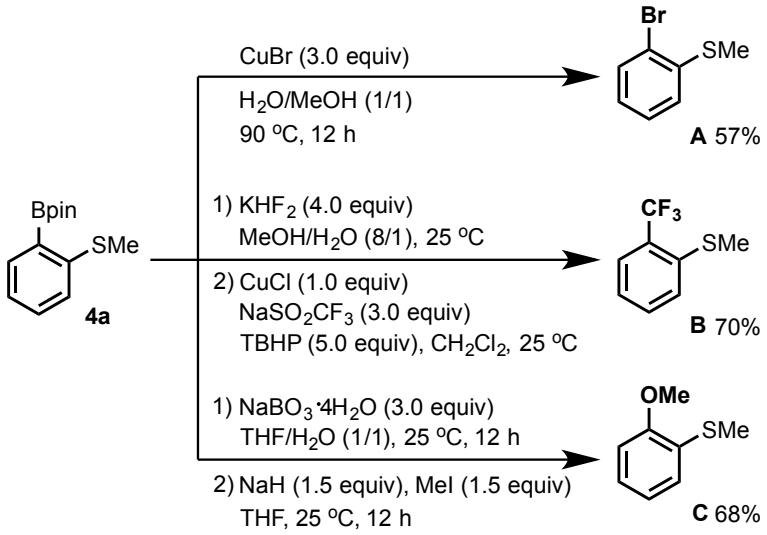


dtbpy: A mixture of *ortho*- and *meta*-borylated products (137 mg, 68% yield, *ortho*/*meta* + *para* = <0.01); *meta*-Isomer **10** was obtained by further purification by GPC (100 mg, 50% yield), yellow oil; ^{1}H NMR

(400 MHz, $CDCl_3$) δ 1.31-1.38 (m, 18H), 2.48 (s, 3H), 4.19-4.27 (m, 4H), 7.17 (s, 1H), 7.31 (s, 1H), 7.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 16.1, 16.2, 25.1, 65.2, 65.3, 84.3, 121.6 (d, J = 4.8 Hz), 123.5 (d, J = 5.7 Hz), 129.5, 140.0, 150.8; IR (KBr, ν / cm^{-1}) 2979, 1567, 1349, 1210, 1143, 1024, 826, 701; HRMS (ESI^+) Calcd for $C_{17}H_{28}BO_5PS_2Na$ ([M+Na]$^+$) 441.1101, Found 441.1122.

Transformations of a boryl group of borylated product 4a.

We investigated further transformations of the boryl group of borylated product **4a** (Scheme S1). The boryl group of **4a** was converted to a bromine atom and trifluoromethyl and methoxy groups.



Scheme S1. Transformations of a boryl group of borylated product **4a**

Synthesis of (2-bromophenyl)(methyl)sulfane (A).

A solution of $CuBr_2$ (268 mg, 1.20 mmol, 3.0 equiv) in H_2O (1.5 mL) was added to a solution of **4a** (100 mg, 0.400 mmol) in MeOH (3.5 mL). The mixture was stirred at reflux for 24 h and the reaction mixture was diluted with dichloromethane (5.0 mL). The organic layer was dried with $MgSO_4$, the mixture was filtered, and the filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (10/1) as an eluent to give **A** as a colorless oil. Yield: (46 mg, 57%); ^1H NMR (400 MHz, $CDCl_3$) δ 2.81 (s, 3H), 7.35 (ddd, J = 7.8, 7.8, 1.8 Hz, 1H), 7.55-7.60 (m, 2H), 7.93 (d, J = 7.8 Hz, 1H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 42.1, 118.7, 125.9, 129.0, 132.5, 133.2, 145.5; IR (KBr, ν / cm^{-1}) 3474, 1447, 1093, 1057, 1014, 758.

Synthesis of methyl(2-(trifluoromethyl)phenyl)sulfane (B).

A mixture of **4a** (100 mg, 0.400 mmol), KHF_2 (125 mg, 1.60 mmol, 4.0 equiv) in MeOH/H_2O (8/1) was stirred at room temperature for 12 h. Then the mixture was concentrated under vacuum conditions, diluted with hot acetone (10 mL), and filtered. The filtrate was washed with hot acetone (2 x 2 mL). The solution was concentrated to give a crude product, which was used in the next step without purification.

A mixture of the crude product, $NaSO_2CF_3$ (207 mg, 1.20 mmol), $NaHCO_3$ (33.6 mg, 0.400 mmol), and CuCl (39.6 mg, 0.400 mmol) in CH_2Cl_2 (5 mL) was cooled to 0 °C, then TBHP (70% solution in water, 220 μL, 2.0 mmol) was added under vigorous stirring, and the stirring was continued at 25 °C for overnight. The reaction mixture was washed with water and the organic layer was dried with Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using hexane as an eluent to give **B** as a colorless oil. Yield: (54 mg, 70%); ^1H NMR (400 MHz, $CDCl_3$) δ 2.55 (s, 3H), 7.26-7.29 (m, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.49 (dd, *J* = 7.8, 7.3 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 120.0 (q, *J* = 139 Hz), 124.9, 126.8 (q, *J* = 6.0 Hz), 127.6, 128.3 (q, *J* = 15.5 Hz), 132.2, 138.5; IR (KBr, ν / cm^{-1}) 1593, 1441, 1313, 1256, 1172, 1115, 1034, 759.

Synthesis of (2-methoxyphenyl)(methyl)sulfane (C).

A round bottom flask was charged with **4a** (1.6 g, 6.4 mmol), $NaBO_3/4H_2O$ (2.90 g, 19.2 mmol), and THF/H_2O (1/1, 30 mL). Then the mixture was stirred at 25 °C for 2 h. The precipitate was filtered, the mixture was extracted with ethyl acetate, and the organic layer was concentrated in vacuo to give a crude product.

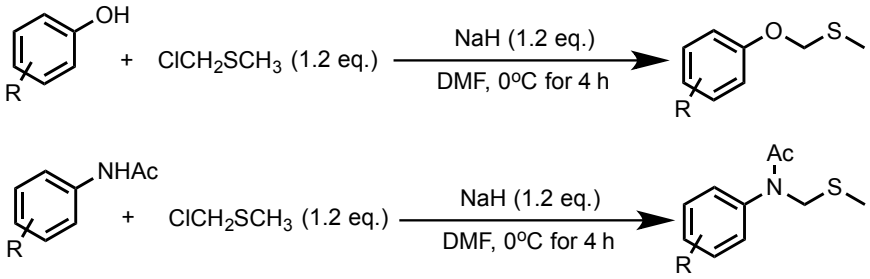
A mixture of the crude product, NaH (329 mg, 9.60 mmol), and THF (20 mL) was cooled to 0 ^oC, and MeI (0.6 mL, 9.6 mmol) was added to the mixture. The mixture was stirred at 25 °C for 5 h. The reaction mixture was concentrated in vacuo and extracted with CH_2Cl_2 (15 mL). The organic solvent was removed in vacuo to give a crude product, which was purified by column chromatography on silica gel to give **C** a colorless oil. Yield: (0.67 g, 68%); ^1H NMR (400 MHz, $CDCl_3$) δ 2.74 (s, 3H), 3.86 (s,

3H), 6.89 (d, *J* = 8.2 Hz, 1H), 7.14 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.40 (dd, *J* = 8.2, 7.8 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.3, 55.8, 110.7, 121.8, 124.7, 132.1, 133.0, 154.9; IR (KBr, ν / cm^{-1}) 2361, 1587, 1476, 1273, 1239, 1027, 758.

2. Development of Iridium/Bipyridine-Catalyzed *ortho*-Selective C-H Boylation of Phenol and Aniline Derivatives

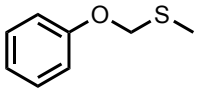
General. All reactions were carried out in a dry and degassed solvent under an argon atmosphere. Reactions were monitored by thin-layer chromatography (TLC) visualizing with UV-light (254 nm). Organic solutions were concentrated under reduced pressure using a rotary evaporator (30 °C, <50 torr). NMR spectra were recorded on 500 MHz (500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR) and 400 MHz (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectrometers. Proton and carbon chemical shifts are reported relative to the solvent used as an internal reference. In ^{13}C NMR, signals of carbons adjacent to a boron atom were not observed because of the quadrupolar relaxation. Infrared (IR) spectra were recorded on Fourier transform infrared spectrophotometer. ESI-MS spectra were measured on a spectrometer for HRMS.

General procedure for the preparation of phenol and aniline derivatives 11a-11t



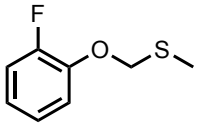
To a solution of a phenol or acetanilide derivative (32.0 mmol) in DMF (25.0 mL), NaH (38.0 mmol, 1.2 equiv) was added slowly at 0 °C. After stirring for 1.5 h at the same temperature, chloromethyl methyl sulfide (38.0 mmol, 1.2 equiv) was added dropwise. The mixture was then stirred for 2.5 h and slowly warmed to room temperature. After removal of the solvent under vacuum, the mixture was extracted with EtOAc. The organic layer was separated, dried over Na_2SO_4, filtered, and the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 10/1).

Methyl(phenoxymethyl)sulfane (11a).



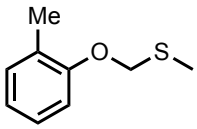
Yield: 60%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23 (s, 3H), 5.12 (s, 2H), 6.92-6.99 (m, 3H), 7.28-7.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 72.3, 115.9, 121.7, 129.4, 157.0.

(2-Fluorophenoxy)methyl)(methyl)sulfane (11b).



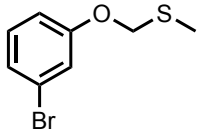
Yield: 88%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3H), 5.23 (s, 2H), 6.98-7.13 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 74.5 (d, J = 1.9 Hz), 116.4 (d, J = 19.0 Hz), 118.2 (d, J = 1.9 Hz), 122.7 (d, J = 6.7 Hz), 124.2 (d, J = 3.8 Hz), 144.5 (d, J = 10.5 Hz), 153.8 (d, J = 250 Hz).

Methyl((*o*-tolyloxy)methyl)sulfane (11c).



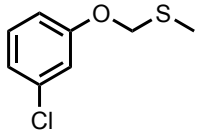
Yield: 74%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 2.27 (s, 3H), 5.18 (s, 2H), 6.89 (d, J = 8.7 Hz, 1H), 6.92 (d, J = 7.8 Hz, 1H), 7.15-7.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 16.3, 72.4, 112.9, 121.4, 126.6, 127.8, 130.9, 155.1.

(3-Bromophenoxy)methyl)(methyl)sulfane (11d).



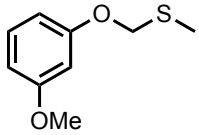
Yield: 65%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H), 5.12 (s, 2H), 6.88-6.90 (m, 1H), 7.12-7.18 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 72.5, 114.7, 119.3, 122.7, 124.8, 130.5, 155.7.

(3-Chlorophenoxy)methyl)(methyl)sulfane (11e).



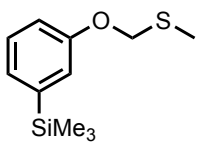
Yield: 79%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 3H), 5.17 (s, 2H), 6.87-6.89 (m, 1H), 6.99-7.01 (m, 2H), 7.24 (dd, J = 7.8, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 72.5, 114.2, 116.4, 121.9, 130.2, 134.8, 157.7.

(3-Methoxyphenoxy)methyl)(methyl)sulfane (11f).



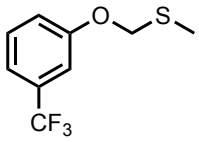
Yield: 68%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.84 (s, 3H), 5.18 (s, 2H), 6.59-6.63 (m, 3H), 7.24 (dd, J = 8.2, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 55.3, 72.4, 102.4, 107.3, 107.8, 129.9, 158.3, 160.7.

Trimethyl(3-((methylthio)methoxy)phenyl)silane (11g).



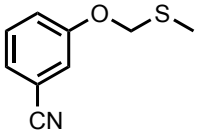
Yield: 72%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.24 (s, 9H), 2.23 (s, 3H), 5.13 (s, 2H), 6.89-6.92 (m, 1H), 7.07-7.08 (m, 1H), 7.12-7.14 (m, 1H), 7.26 (dd, *J* = 8.2, 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ –1.2, 14.7, 72.3, 115.7, 120.9, 126.6, 128.9, 142.4, 156.5.

Methyl((3-(trifluoromethyl)phenoxy)methyl)sulfane (11h).



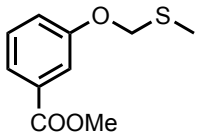
Yield: 62%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 5.25 (s, 2H), 7.19 (d, *J* = 8.3 Hz, 1H), 7.26 (s, 1H), 7.32-7.34 (m, 1H), 7.47 (dd, *J* = 8.3, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 72.3, 112.9 (q, *J* = 3.8 Hz), 118.3 (q, *J* = 3.8 Hz), 119.2, 123.8 (q, *J* = 290 Hz), 130.0, 131.4 (q, *J* = 34.3 Hz), 157.1.

3-((Methylthio)methoxy)benzonitrile (11i).



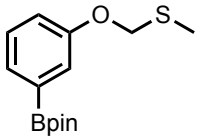
Yield: 77%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 5.22 (d, 2H), 7.23-7.26 (m, 2H), 7.31-7.36 (m, 1H), 7.43-7.47 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 72.6, 113.2, 118.5, 119.1, 120.9, 125.4, 130.3, 157.0.

Methyl 3-((methylthio)methoxy)benzoate (11j).



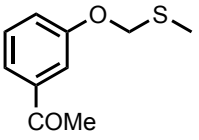
Yield: 62%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H), 3.91 (s, 3H), 5.19 (s, 2H), 7.14 (d, *J* = 8.7 Hz, 1H), 7.34 (dd, *J* = 8.3, 8.3 Hz, 1H), 7.61 (s, 1H), 7.68 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 52.2, 72.4, 116.4, 121.1, 122.9, 129.4, 131.4, 156.9, 166.5.

4,4,5,5-Tetramethyl-2-(3-((methylthio)methoxy)phenyl)-1,3,2-dioxaborolane (11k).



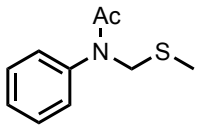
Yield: 58%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.24 (s, 3H), 5.17 (s, 2H), 7.05 (d, *J* = 7.3 Hz, 1H), 7.29 (dd, *J* = 7.8, 7.3 Hz, 1H), 7.37 (s, 1H), 7.44 (d, *J* = 6.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 24.8, 72.3, 83.9, 119.5, 121.2, 128.2, 129.0, 156.5.

1-(3-((Methylthio)methoxy)phenyl)ethan-1-one (11l).



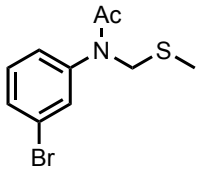
Yield: 70%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (s, 3H), 2.59 (s, 3H), 5.18 (s, 2H), 7.14 (d, *J* = 8.3 Hz, 1H), 7.37 (dd, *J* = 8.2, 7.8 Hz, 1H), 7.53 (s, 1H), 7.57 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 26.7, 72.4, 114.9, 121.1, 122.0, 129.6, 138.5, 157.2, 197.7.

***N*-((Methylthio)methyl)-*N*-phenylacetamide (11m).**



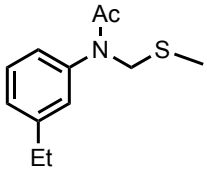
Yield: 74%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.86 (s, 3H), 2.15 (s, 3H), 4.83 (s, 2H), 7.24-7.26 (m, 2H), 7.38-7.44 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 22.7, 52.5, 128.3, 128.4, 129.7, 141.8, 170.7.

***N*-(3-Bromophenyl)-*N*-((methylthio)methyl)acetamid*e* (11n).**



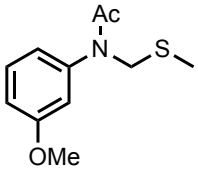
Yield: 84%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88 (s, 3H), 2.16 (s, 3H), 4.81 (s, 2H), 7.21 (d, *J* = 7.8 Hz, 1H), 7.30 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.44 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 22.7, 52.5, 122.9, 127.3, 130.9, 131.6, 131.7, 143.1, 170.4.

***N*-(3-Ethylphenyl)-*N*-((methylthio)methyl)acetamide (11o).**



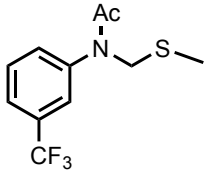
Yield: 75%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (t, *J* = 7.8 Hz, 3H), 1.87 (s, 3H), 2.16 (s, 3H), 2.66 (q, *J* = 7.8 Hz, 3H), 4.83 (s, 2H), 7.05-7.08 (m, 2H), 7.20 (d, *J* = 7.8 Hz, 1H), 7.32 (dd, *J* = 7.8, 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 14.9, 22.1, 28.1, 51.9, 125.1, 127.2, 127.3, 129.0, 141.3, 145.5, 170.1.

***N*-(3-Methoxyphenyl)-*N*-((methylthio)methyl)acetamide (11p).**



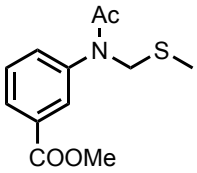
Yield: 66%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.89 (s, 3H), 2.16 (s, 3H), 3.83 (s, 3H), 4.82 (s, 2H), 6.79-6.86 (m, 2H), 6.91 (d, *J* = 8.7 Hz, 1H), 7.31 (dd, *J* = 8.3, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 22.6, 52.5, 55.4, 113.6, 114.3, 120.6, 130.3, 143.0, 160.5, 170.7.

***N*-((Methylthio)methyl)-*N*-(3-(trifluoromethyl)phenyl)acetamide (11q).**



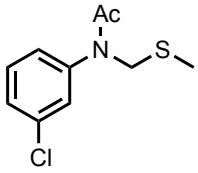
Yield: 69%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.85 (s, 3H), 2.16 (s, 3H), 4.82 (s, 2H), 7.46 (d, *J* = 7.3 Hz, 1H), 7.53 (s, 1H), 7.57 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.64 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 22.7, 52.4, 120.6 (q, *J* = 276 Hz), 125.3, 125.4, 130.3, 131.8 (q, *J* = 33.3 Hz), 132.1, 142.3, 170.2.

Methyl 3-(*N*-((methylthio)methyl)acetamido)benzoate (1r).



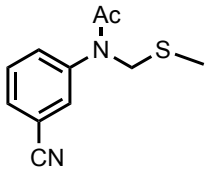
Yield: 80%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 (s, 3H), 2.13 (s, 3H), 3.91 (s, 3H), 4.82 (s, 2H), 7.43 (d, *J* = 8.7 Hz, 1H), 7.49-7.53 (m, 1H), 7.89 (s, 1H), 8.02 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 22.6, 52.3, 52.4, 129.4, 129.7, 130.0, 131.8, 133.0, 141.9, 165.9, 170.3.

***N*-(3-Chlorophenyl)-*N*-((methylthio)methyl)acetamide (11s).**



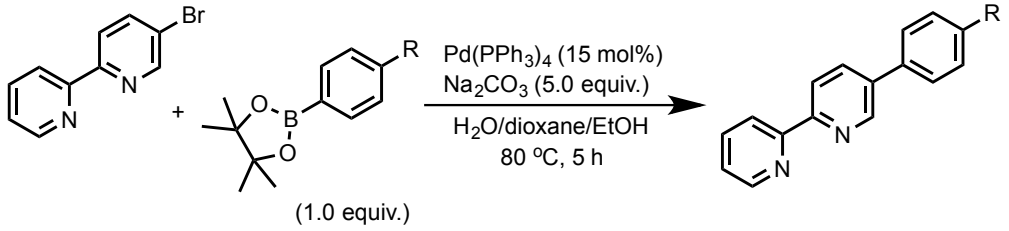
Yield: 70%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88 (s, 3H), 2.17 (s, 3H), 4.82 (s, 2H), 7.15-7.18 (m, 1H), 7.28-7.29 (m, 1H), 7.38-7.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 22.7, 52.5, 126.9, 128.7, 128.8, 130.6, 135.1, 142.9, 170.4.

***N*-(3-Cyanophenyl)-*N*-((methylthio)methyl)acetamide (1t).**



Yield: 78%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80 (s, 3H), 2.09 (s, 3H), 4.76 (s, 2H), 7.47-7.50 (m, 1H), 7.52-7.56 (m, 2H), 7.63 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.9, 22.5, 52.1, 113.6, 117.4, 130.6, 131.8, 132.0, 133.2, 142.3, 169.8.

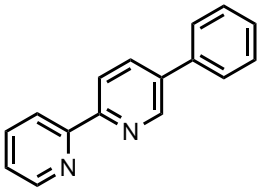
General procedure for the synthesis of ligands L4-L9.



5-Bromo-2,2'-bipyridine (1.00 g, 4.27 mmol), *para*-substituted 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (4.27 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (745 mg, 0.640 mmol), and sodium carbonate (2.30 g, 21.5 mmol) were added into a 50 mL two-necked flask quipped with a reflux condenser. After addition of 1,4-dioxane (20 mL), EtOH (12 mL), and water (12 mL), the mixture was refluxed for 4 h. The reaction mixture was cooled to room temperature and extracted with EtOAc (20 mL) two times. The organic phase was separated and washed with H_2O (30 mL), and dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed under vacuum and the mixture was

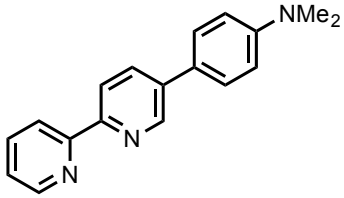
purified by column chromatography on silica gel.

5-Phenyl-2,2'-bipyridine (L4).



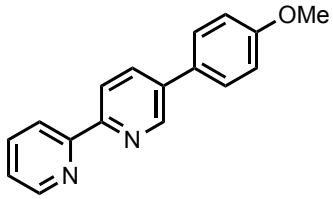
Yield: 88%; colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.33 (m, 1H), 7.43-7.53 (m, 3H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.82-7.86 (m, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 8.43-7.49 (m, 2H), 8.69-8.71 (m, 1H), 8.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.9, 121.0, 123.7, 127.1, 128.2, 129.1, 135.2, 136.5, 136.9, 137.6, 147.6, 149.2, 155.0, 155.9; IR (KBr, ν/cm^{-1}) 3047, 1549, 1458, 1374, 856, 797, 750, 696; HRMS (ESI^{+}) Calcd for $C_{16}H_{12}N_2Na^{+}$ ([M+Na]$^{+}$) 255.0893, Found 255.0898.

4-([2,2'-Bipyridin]-5-yl)-*N*,*N*-dimethylaniline (L5).



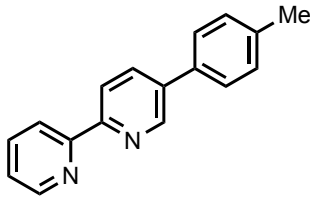
Yield: 70%; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.02 (s, 6H), 6.83-6.85 (m, 2H), 7.28-7.31 (m, 1H), 7.57-7.59 (m, 2H), 7.80-7.84 (m, 1H), 7.96 (dd, *J* = 8.7, 2.3 Hz, 1H), 8.40 (d, *J* = 8.7 Hz, 2H), 8.68-8.69 (m, 1H), 8.90-8.91 (m, 1H); ^{13}C NM (100 MHz, $CDCl_3$) δ 40.4, 112.8, 120.8, 120.9, 123.3, 125.0, 127.6, 134.0, 136.4, 136.9, 146.8, 149.1, 150.4, 153.5, 156.1; IR (KBr, ν/cm^{-1}) 2884, 1610, 1459, 1363, 1211, 945, 860, 794, 632; HRMS (ESI^{+}) Calcd for $C_{18}H_{17}N_3Na^{+}$ ([M+Na]$^{+}$) 298.1315, Found 298.1318.

5-(4-Methoxyphenyl)-2,2'-bipyridine (L6).



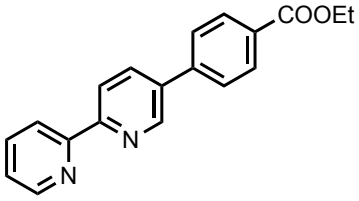
Yield: 90%; colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 (s, 3H), 7.02 (dd, *J* = 8.7, 3.2 Hz, 2H), 7.30-7.33 (m, 1H), 7.59-7.62 (m, 2H), 7.82-7.85 (m, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 8.42-8.46 (m, 2H), 8.70-8.71 (m, 1H), 8.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 114.5, 120.9, 123.5, 128.1, 129.9, 134.6, 136.0, 136.9, 147.1, 149.2, 154.2, 156.0, 159.8; IR (KBr, ν/cm^{-1}) 2989, 1605, 1521, 1454, 1370, 1282, 1032, 830, 747, 692; HRMS (ESI^{+}) Calcd for $C_{17}H_{14}N_2ONa^{+}$ ([M+Na]$^{+}$) 285.0998, Found 285.0998.

5-(*p*-Tolyl)-2,2'-bipyridine (L7).



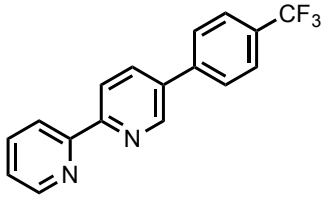
Yield: 71%; colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 7.29-7.32 (m, 3H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.80-7.85 (m, 1H), 7.99-8.02 (m, 1H), 8.42-8.46 (m, 2H), 8.69-8.71 (m, 1H), 8.91-8.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 120.9, 121.0, 123.6, 126.9, 129.8, 134.6, 135.0, 136.4, 136.9, 138.1, 147.4, 149.2, 154.6, 155.9; IR (KBr, ν/cm^{-1}) 3046, 1587, 1456, 1371, 1241, 1133, 1089, 1027, 792, 648; HRMS (ESI^{+}) Calcd for $C_{17}H_{14}N_2Na^{+}$ ([M+Na]$^{+}$) 269.1049, Found 269.1038.

Ethyl 4-([2,2'-bipyridin]-5-yl)benzoate (L8).



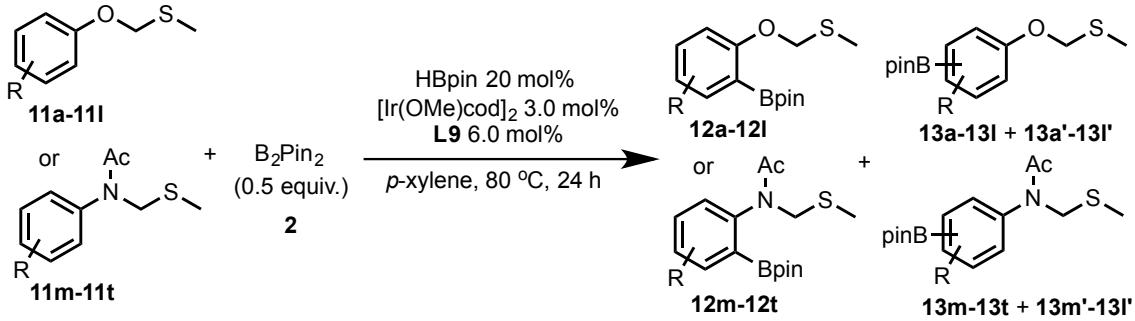
Yield: 80%; colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (t, *J* = 7.1 Hz, 3H), 4.40 (q, *J* = 7.1 Hz, 4H), 7.32-7.36 (m, 1H), 7.71-7.74 (d, *J* = 8.7 Hz, 2H), 7.82-7.87 (m, 1H), 8.05 (dd, *J* = 8.2, 2.3 Hz, 1H), 8.16-8.19 (d, *J* = 8.7 Hz, 2H), 8.44 (d, *J* = 8.2 Hz, 1H), 8.50 (d, *J* = 8.2 Hz, 1H), 8.70-8.72 (m, 1H), 8.94-8.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 61.1, 121.0, 121.1, 123.9, 126.9, 130.1, 130.3, 135.3, 135.4, 137.0, 141.9, 147.7, 149.3, 155.5, 155.6, 166.2; IR (KBr, ν/cm^{-1}) 3396, 2981, 1722, 1590, 1437, 1275, 1125, 1025, 843, 765, 645; HRMS (ESI^{+}) Calcd for $C_{19}H_{16}N_2O_2Na^{+}$([M+Na]$^{+}$) 327.1104, Found 327.1100.

5-(4-(Trifluoromethyl)phenyl)-2,2'-bipyridine (L9).



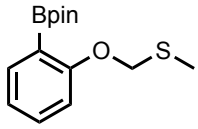
Yield: 73%; colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.35 (m, 1H), 7.75-7.76 (m, 4H), 7.82-7.87 (m, 1H), 8.01-8.04 (m, 1H), 8.43 (d, *J* = 7.8 Hz, 1H), 8.50 (d, *J* = 8.2 Hz, 1H), 8.70-8.71 (m, 1H), 8.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.1, 121.2 , 124.0, 124.1 (q, *J* = 275 Hz), 126.0 (q, *J* = 3.8 Hz), 127.4, 130.4, 135.0, 135.4, 137.0, 141.2, 147.6, 149.3, 155.5, 155.8; IR (KBr, ν/cm^{-1}) 3019, 1588, 1437, 1329, 1113, 1072, 840, 754, 658; HRMS (ESI^{+}) Calcd for $C_{17}H_{11}F_3N_2H^{+}$ ([M+H]$^{+}$) 301.0947, Found 301.0948.

General procedure for *ortho*-selective C-H borylation of phenol and aniline derivatives 11a-11t.



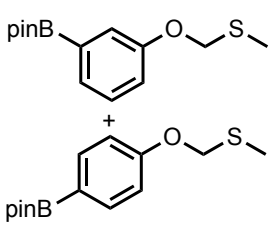
A phenol(**11a**, 0.500 mmol) or aniline derivative (**11t**, 0.500 mmol), B_2pin_2 (**2**, 63.5 mg, 0.250 mmol, 0.50 equiv), $[Ir(OMe)(cod)]_2$ (9.94 mg, 0.0150 mmol, 3.0 mol%), ligand **3a** (11.1 mg, 0.0300 mmol, 6.0 mol%), and *p*-xylene (1.5 mL) were added into a 10 mL sealed tube. The mixture was stirred at 55 °C for 24 h. Then, the solvent was removed under vacuum, and C-H borylation products **4** and **5** were separated by column chromatography on silica gel (hexane/EtOAc = 10/1).

4,4,5,5-Tetramethyl-2-(2-((methylthio)methoxy)phenyl)-1,3,2-dioxaborolane (12a).



L9: A mixture of *ortho*-, *meta*- and *para*-borylated products (126 mg, 90% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12a** was obtained by further purification (115 mg, 82% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 2.23 (s, 3H), 5.18 (s, 2H), 6.91 (d, J = 7.3 Hz, 1H), 7.02 (d, J = 6.8 Hz, 1H), 7.41 (d, J = 5.9 Hz, 1H), 7.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 24.8, 73.0, 83.4, 114.6, 121.7, 132.2, 136.8, 161.5; IR (KBr, ν/cm^{-1}) 2978, 1574, 1357, 1271, 1198, 1019, 850, 797; HRMS (ESI$^+$) Calcd for $C_{14}H_{21}BO_3SNa^+$ ([M+Na]$^+$) 303.1197, Found 303.1208.

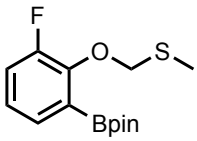
4,4,5,5-Tetramethyl-(2-((methylthio)methoxy)phenyl)-1,3,2-dioxaborolane (13a+13a′).



dtbpy: A mixture of *ortho*-, *meta*- and *para*-borylated products (123 mg, 88% yield, *ortho* / *meta* + *para* = 0.83); a mixture of *meta and para*-isomers (**13a+13a′**) was obtained by further purification by GPC (61.0 mg, 44% yield), colorless; *meta*-isomer **13a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.25 (s, 3H), 5.17 (s, 2H), 7.05 (d, J = 7.3 Hz,

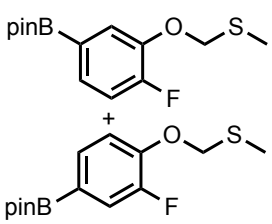
1H), 7.29 (dd, *J* = 7.8, 7.3 Hz, 1H), 7.37 (s, 1H), 7.44 (d, *J* = 6.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 24.8, 72.3, 83.9, 119.5, 121.2, 128.2, 129.0, 156.5; *para*-isomer **13a′**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 2.25 (s, 3H), 5.16 (s, 2H), 6.93 (d, *J* = 7.8 Hz, 2H), 7.75 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 24.8, 72.0, 83.6, 115.1, 136.4, 159.6; IR (KBr, ν / cm^{-1}) 2977, 1603, 1359, 1143, 1091, 994, 860, 743, 654; HRMS (ESI^+) Calcd for $C_{14}H_{21}BO_3SNa^+$ ($[M+Na]^+$) 303.1197, Found 303.1182.

2-(3-Fluoro-2-((methylthio)methoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (12b).



L9: A mixture of *ortho*-, *meta*- and *para*-borylated products (104 mg, 70% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12b** was obtained by further purification (93.0 mg, 62% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.30 (s, 3H), 5.22 (s, 2H), 7.06-7.09 (m, 1H), 7.15-7.20 (m, 1H), 7.48 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3 (d, *J* = 1.4 Hz), 24.8, 78.7 (d, *J* = 5.2 Hz), 83.9 (d, *J* = 3.3 Hz), 119.4 (d, *J* = 20 Hz), 124.4 (d, *J* = 6.6 Hz), 131.6 (d, *J* = 3.8 Hz), 148.9 (d, *J* = 10.5 Hz), 155.7 (d, *J* = 251 Hz); IR (KBr, ν/cm^{-1}) 2979, 1633, 1455, 966, 852, 741, 669; HRMS (ESI^+) Calcd for $C_{14}H_{20}BFO_3SNa^+$ ($[M+Na]^+$) 321.1102, Found 321.1088.

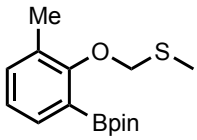
(3-Fluoro-2-((methylthio)methoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (13b+13b′).



dtbpy: A mixture of *ortho*-, *meta*- and *para*-borylated products (75.0 mg, 50% yield, *ortho* / *meta* + *para* = 0.83); a mixture of *meta*- *and para*-isomers (**13b+13b′**) was obtained by further purification by GPC (35.0 mg, 24% yield), colorless oil; *meta*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.27 (s, 3H), 5.25 (s, 2H), 7.06 (m, 1H), 7.26 (s, 1H), 7.44 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 24.8, 74.3, 84.0, 116.0 (d, *J* = 18 Hz), 123.8 (d, *J* = 2.4 Hz), 129.8 (d, *J* = 7.6 Hz), 144.1 (d, *J* = 10.4 Hz), 156.0 (d, *J* = 255 Hz) *para*-isomer: δ 1.33 (s, 12H), 2.26 (s, 3H), 5.24 (s, 2H), 7.00-7.04 (m, 1H), 7.50-7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 24.8, 73.9 (d, *J* = 1.4 Hz), 83.9, 116.8 (d, *J* = 1.4 Hz), 122.1 (d, *J* = 17.2 Hz), 131.0 (d, *J* = 3.8 Hz), 147.0 (d,

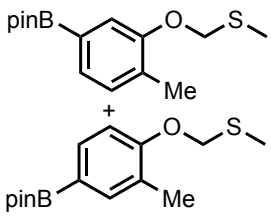
J = 10.9 Hz), 153.2 (d, *J* = 250 Hz); IR (KBr, ν / cm^{-1}) 2978, 2359, 1734, 1599, 1417, 853, 760, 681; HRMS (ESI^+) Calcd for $C_{14}H_{20}BFO_3SNa^+$ ($[M+Na]^+$) 321.1102, Found 321.1102.

4,4,5,5-Tetramethyl-2-(3-methyl-2-((methylthio)methoxy)phenyl)-1,3,2-dioxaborolane (12c).



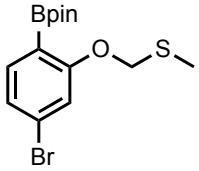
L9: A mixture of *ortho*-, *meta* and *para*-borylated products (101 mg, 69% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12c** was obtained by further purification (98 mg, 67% yield), colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 2.30 (s, 3H), 2.35 (s, 3H), 5.08 (s, 2H), 7.02 (dd, *J* = 7.8, 7.3 Hz, 1H), 7.28-7.30 (m, 1H), 7.59 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 16.9, 24.8, 79.4, 83.7, 123.9, 131.3, 134.4, 134.7, 161.6; IR (KBr, ν/cm^{-1}) 2977, 1596, 1418, 980, 853, 784, 668; HRMS (ESI^+) Calcd for $C_{15}H_{23}BO_3SNa^+$ ($[M+Na]^+$) 317.1353, Found 317.1354.

4,4,5,5-Tetramethyl-(3-methyl-2-((methylthio)methoxy)phenyl)-1,3,2-dioxaborolane (13c+13c′).



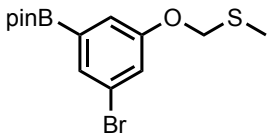
dtbpy: A mixture of *ortho*-, *meta*-, and *para*-borylated products (109 mg, 74% yield, *ortho* / *meta* + *para* = 0.76); a mixture of *meta*- *and para*-isomers (**13c+13c′**) was obtained by further purification by GPC (58.0 mg, 40% yield), colorless oil; *meta*-isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.26 (s, 3H), 2.28 (s, 3H), 5.21 (s, 2H), 7.16 (d, *J* = 7.3 Hz, 1H), 7.28 (s, 1H), 7.37 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 16.6, 24.8, 72.4, 83.7, 118.3, 128.2, 130.6, 131.5, 154.9; *para*-isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 2.25 (s, 6H), 5.19 (s, 2H), 6.86 (d, *J* = 8.2 Hz, 1H), 7.62-7.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 16.0, 24.8, 72.0, 83.5, 111.9, 127.0, 133.8, 137.5, 157.7; IR (KBr, ν / cm^{-1}) 2977, 1604, 1357, 1132, 995, 855, 735, 670; HRMS (ESI^+) Calcd for $C_{15}H_{23}BO_3SNa^+$ ($[M+Na]^+$) 317.1353, Found 317.1352.

2-(4-Bromo-2-((methylthio)methoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (12d).



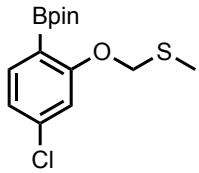
L9: A mixture of *ortho*- and *meta*-borylated products (147 mg, 82% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12d** was obtained by further purification of the crude mixture by GPC (140 mg, 78% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 2.27 (s, 3H), 5.15 (s, 2H), 7.06-7.07 (m, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 24.8, 73.1, 83.6, 117.9, 124.8, 126.1, 138.0, 162.2; IR (KBr, ν/cm^{-1}) 2977, 1558, 1397, 1143, 843, 668; HRMS (ESI^{+}) Calcd for $C_{14}H_{20}BBrO_3SNa^{+}$ ([M+Na]$^{+}$) 381.0302, Found 381.0284.

2-(3-Bromo-5-((methylthio)methoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (13d).



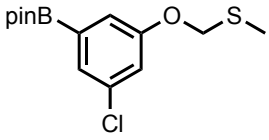
dtbpy: A mixture of *ortho*- and *meta*-borylated products (120 mg, 67% yield, *ortho*/*meta* + *para* = < 0.1); *meta*-Isomer (**13d**) were obtained by further purification of the crude mixture by GPC (106 mg, 59% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 12H), 2.22 (s, 3H), 5.12 (s, 2H), 7.18 (s, 1H), 7.26 (s, 1H), 7.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 24.8, 72.5, 84.2, 120.0, 122.4, 122.6, 130.7, 157.3; IR (KBr, ν/cm^{-1}) 2977, 1558, 1417, 1143, 1048, 851, 701; HRMS (ESI^{+}) Calcd for $C_{14}H_{20}BBrO_3SNa^{+}$ ([M+Na]$^{+}$) 381.0302, Found 381.0284.

2-(4-Chloro-2-((methylthio)methoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (12e).



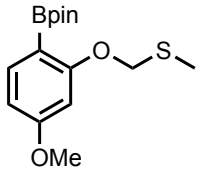
L9: A mixture of *ortho*- and *meta*-borylated products (144 mg, 92% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12e** was obtained by further purification of the crude mixture by GPC (130 mg, 83% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 2.27 (s, 3H), 5.15 (s, 2H), 6.90 (s, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 24.8, 73.0, 83.6, 115.0, 121.8, 137.7, 137.8, 162.2; IR (KBr, ν/cm^{-1}) 2978, 1591, 1402, 1206, 1145, 1061, 996, 853, 652; HRMS (ESI^{+}) Calcd for $C_{14}H_{20}BClO_3SNa^{+}$ ([M+Na]$^{+}$) 337.0807, Found 337.0798.

2-(3-Chloro-5-((methylthio)methoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (13e).



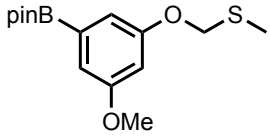
dtbpy: A mixture of *ortho*- and *meta*-borylated products (133 mg, 85% yield, *ortho* / *meta* + *para* = 0.45); *meta*-isomer (**13e**) was obtained by further purification of the crude mixture by GPC (86 mg, 55% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 2.25 (s, 3H), 5.16 (s, 2H), 7.06 (s, 1H), 7.26 (s, 1H), 7.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 24.8, 72.4, 84.2, 119.5, 119.6, 127.9, 134.5, 157.2; IR (KBr, ν/cm^{-1}) 2987, 1566, 1471, 1143, 1019, 854, 701; HRMS (ESI$^+$) Calcd for $C_{14}H_{20}BClO_3SNa^+$ ([M+Na]$^+$) 337.0807, Found 337.0801.

2-(4-Methoxy-2-((methylthio)methoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (12f).



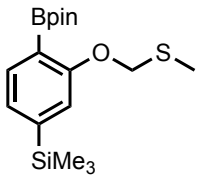
L9: A mixture of *ortho*- and *meta*-borylated products (115 mg, 74% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12f** was obtained by further purification of the crude mixture by GPC (110 mg, 71% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 12H), 2.27 (s, 3H), 3.79 (s, 3H), 5.14 (s, 2H), 6.46-6.47 (m, 1H), 6.54 (d, *J* = 8.7 Hz, 1H), 7.65 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 24.8, 55.3, 73.1, 83.1, 101.8, 106.5, 138.3, 163.2, 163.4; IR (KBr, ν/cm^{-1}) 2976, 1604, 1351, 1146, 1035, 860, 659; HRMS (ESI$^+$) Calcd for $C_{15}H_{23}BNO_4SNa^+$ ([M+Na]$^+$) 333.1302, Found 333.1287.

2-(3-Methoxy-5-((methylthio)methoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (13f).



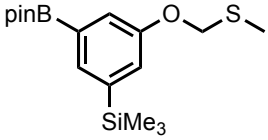
dtbpy: A mixture of *ortho*- and *meta*-borylated products (85.0 mg, 55% yield, *ortho* / *meta* + *para* = 2.0); *meta*-isomer (**13f**) was obtained by further purification of the crude mixture by GPC (17.0 mg, 11% yield); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.24 (s, 3H), 3.81 (s, 3H), 5.14 (s, 2H), 6.63 (s, 1H), 6.98-6.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 24.8, 55.4, 72.3, 83.9, 106.3, 112.5, 113.6, 157.8, 160.3; IR (KBr, ν/cm^{-1}) 2977, 1586, 1371, 1145, 1025, 966, 850, 704; HRMS (ESI$^+$) Calcd for $C_{15}H_{23}BNO_4SNa^+$ ([M+Na]$^+$) 333.1302, Found 333.1289.

Trimethyl(3-((methylthio)methoxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)silane (12g).



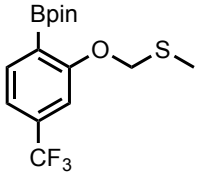
L9: A mixture of *ortho*- and *meta*-borylated products (141 mg, 80% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12g** was obtained by further purification of the crude mixture by GPC (122 mg, 69% yield), colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.26 (s, 9H), 1.34 (s, 12H), 2.28 (s, 3H), 5.19 (s, 2H), 7.06 (s, 1H), 7.17 (d, *J* = 7.1 Hz, 1H), 7.69 (d, *J* = 7.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -1.30, 14.4, 24.8, 73.5, 83.4, 119.6, 126.7, 136.1, 145.7, 161.1; IR (KBr, ν/cm^{-1}) 2977, 1396, 1202, 1144, 1055, 836; HRMS (ESI^{+}) Calcd for $C_{17}H_{29}BO_3SSiNa^{+}$ ([M+Na]$^{+}$) 375.1592, Found 375.1603.

Trimethyl(3-((methylthio)methoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)silane (13g).



dtbpy: A mixture of *ortho*- and *meta*-borylated products (127 mg, 72% yield, *ortho* / *meta* + *para* = 1.0); *meta*-isomer (**13g**) was obtained by further purification of the crude mixture by GPC (50.0 mg, 28% yield); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.27 (s, 9H), 1.33 (s, 12H), 2.26 (s, 3H), 5.18 (s, 2H), 7.21 (s, 1H), 7.35 (s, 1H), 7.59 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -1.10, 14.6, 24.8, 72.2, 83.8, 121.0, 124.6, 133.1, 141.7, 156.0; IR (KBr, ν/cm^{-1}) 2976, 1540, 1396, 1202, 1144, 1055, 836; HRMS (ESI^{+}) Calcd for $C_{17}H_{29}BO_3SSiNa^{+}$ ([M+Na]$^{+}$) 375.1592, Found 375.1600.

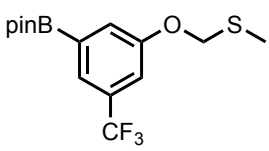
4,4,5,5-Tetramethyl-2-(2-((methylthio)methoxy)-4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (12h).



L9: A mixture of *ortho*- and *meta*-borylated products (150 mg, 86% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12h** was obtained by further purification of the crude mixture by GPC (127 mg, 72% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.27 (s, 3H), 5.19 (s, 2H), 7.11 (s, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 24.8, 73.1, 83.9, 110.8 (q, *J* = 3.8 Hz), 118.0 (q, *J* = 3.8 Hz), 123.8 (q, *J* = 276 Hz), 133.6 (q, *J* = 33 Hz), 137.2, 161.5; IR (KBr, ν/cm^{-1}) 2980, 1595, 1387,

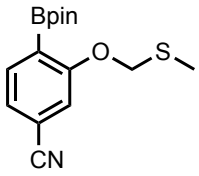
1130, 1019, 857, 743, 685; HRMS (ESI$^+$) Calcd for $C_{15}H_{20}BF_3O_3SNa^+$ ([M+Na]$^+$) 371.1071, Found 371.1075.

4,4,5,5-Tetramethyl-2-(3-((methylthio)methoxy)-5-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (13h).



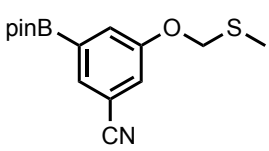
dtbpy: A mixture of *ortho*- and *meta*-borylated products (143 mg, 82% yield, *ortho* / *meta* + *para* = 0.65); *meta*-isomer (**13h**) was obtained by further purification of the crude mixture by GPC (81.0 mg, 46% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.24 (s, 3H), 5.19 (s, 2H), 7.26 (s, 1H), 7.51 (s, 1H), 7.69 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 24.8, 72.4, 84.3, 115.9 (q, *J* = 4.3 Hz), 123.9 (q, *J* = 276 Hz), 124.4 (q, *J* = 3.8 Hz), 131.6 (q, *J* = 33 Hz), 156.6, 161.5; IR (KBr, ν/cm^{-1}) 2980, 1617, 1507, 1387, 1127, 1019, 857, 706, 685; HRMS (ESI$^+$) Calcd for $C_{15}H_{20}BF_3O_3SNa^+$ ([M+Na]$^+$) 371.1071, Found 371.1078.

3-((Methylthio)methoxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (12i).



L9: A mixture of *ortho*- and *meta*-borylated products (109 mg, 71% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12i** was obtained by further purification of the crude mixture by GPC (95.0 mg, 62% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.26 (s, 3H), 5.18 (s, 2H), 7.14 (s, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 24.8, 73.0, 84.2, 115.1, 117.2, 118.7, 125.0, 137.2, 161.1; IR (KBr, ν/cm^{-1}) 2980, 2229, 1583, 1371, 1135, 1036, 847, 698, 620; HRMS (ESI$^+$) Calcd for $C_{15}H_{20}BNO_3SNa^+$ ([M+Na]$^+$) 328.1149, Found 328.1142.

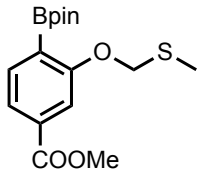
3-((Methylthio)methoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (13i).



dtbpy: A mixture of *ortho*- and *meta*-borylated products (130 mg, 85% yield, *ortho* / *meta* + *para* = 0.35); *meta*-isomer (**13i**) was obtained by further purification of the crude mixture by GPC (92.0 mg, 60% yield), colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 12H), 2.22 (s, 3H), 5.16 (s, 2H),

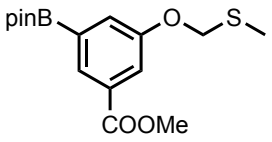
7.26 (s, 1H), 7.55 (s, 1H), 7.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 24.7, 72.4, 84.4, 122.8, 118.4, 121.7, 126.1, 131.4, 156.3; IR (KBr, ν/cm^{-1}) 2978, 2229, 1583, 1378, 1139, 1040, 847, 697, 620; HRMS (ESI$^+$) Calcd for $C_{15}H_{20}BNO_3SNa^+$ ([M+Na]$^+$) 328.1149, Found 328.1158.

Methyl 3-((methylthio)methoxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (12j).



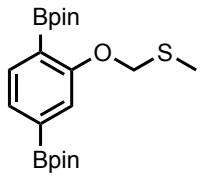
L9: A mixture of *ortho*- and *meta*-borylated products (154 mg, 91% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12j** was obtained by further purification of the crude mixture by GPC (142 mg, 84% yield), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.26 (s, 3H), 3.90 (s, 3H), 5.21 (s, 2H), 7.54 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 24.8, 52.2, 72.7, 83.8, 114.5, 122.4, 133.3, 136.5, 161.3, 166.7; IR (KBr, ν/cm^{-1}) 3446, 2979, 1716, 1559, 1418, 668; HRMS (ESI$^+$) Calcd for $C_{16}H_{23}BO_5SNa^+$ ([M+Na]$^+$) 361.1251, Found 361.1265.

Methyl 3-((methylthio)methoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (13j).



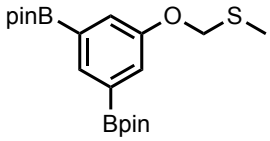
dtbpy: A mixture of *ortho*- and *meta*-borylated products (88.0 mg, 52% yield, *ortho* / *meta* + *para* = 1.8); *meta*-isomer (**13j**) was obtained by further purification of the crude mixture by GPC (19.0 mg, 11% yield), colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.24 (s, 3H), 3.91 (s, 3H), 5.20 (s, 2H), 7.56 (s, 1H), 7.70 (s, 1H), 8.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 24.8, 52.1, 72.4, 84.2, 119.6, 126.5, 129.2, 131.0, 156.5, 166.8; IR (KBr, ν/cm^{-1}) 3446, 2979, 1717, 1559, 1417, 1143, 853, 668; HRMS (ESI$^+$) Calcd for $C_{16}H_{23}BO_5SNa^+$ ([M+Na]$^+$) 361.1251, Found 361.1265.

2,2'-(2-((Methylthio)methoxy)-1,4-phenylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (12k).



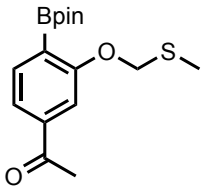
L9: A mixture of *ortho*- and *meta*-borylated products (148 mg, 73% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12k** was obtained by further purification of the crude mixture by GPC (137 mg, 68% yield), colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 1.35 (s, 12H), 2.28 (s, 3H), 5.21 (s, 2H), 7.31 (s, 1H), 7.43 (d, *J* = 7.3 Hz, 1H), 7.68 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 24.8, 72.9, 83.5, 83.9, 119.8, 127.9, 136.1, 161.1; IR (KBr, ν/cm^{-1}) 2977, 1390, 1141, 1033, 966, 847, 712; HRMS (ESI^{+}) Calcd for $C_{20}H_{32}B_2O_5SNa^{+}$ ([M+Na]$^{+}$) 429.2049, Found 429.2029.

2,2'-(5-((Methylthio)methoxy)-1,3-phenylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (13k).



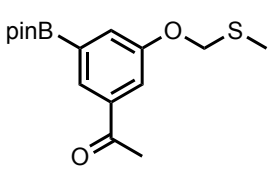
dtbpy: A mixture of *ortho*- and *meta*-borylated products (168 mg, 83% yield, *ortho* / *meta* + *para* = 0.3); *meta*-isomer (**13k**) was obtained by further purification of the crude mixture by GPC (116 mg, 57% yield); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 24H), 2.23 (s, 3H), 5.18 (s, 2H), 7.47 (s, 2H), 7.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 24.8, 72.1, 83.8, 124.8, 134.7, 156.0; IR (KBr, ν/cm^{-1}) 2977, 1316, 1142, 1033, 966, 847, 712; HRMS (ESI^{+}) Calcd for $C_{20}H_{32}B_2O_5SNa^{+}$ ([M+Na]$^{+}$) 429.2049, Found 429.2033.

1-(3-((Methylthio)methoxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one (12l).



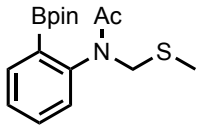
L9: A mixture of *ortho*- and *meta*-borylated products (143 mg, 89% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12l** was obtained by further purification of the crude mixture by GPC (125 mg, 78% yield), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.25 (s, 3H), 2.58 (s, 3H), 5.21 (s, 2H), 7.46 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 24.7, 26.7, 72.7, 83.8, 112.6, 121.6, 136.7, 140.0, 161.5, 197.9; IR (KBr, ν/cm^{-1}) 3434, 2987, 1685, 1559, 1407, 1052, 853, 749, 663; HRMS (ESI^{+}) Calcd for $C_{16}H_{23}BO_4SNa^{+}$ ([M+Na]$^{+}$) 345.1302, Found 345.1294.

1-(3-((Methylthio)methoxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one (13l).



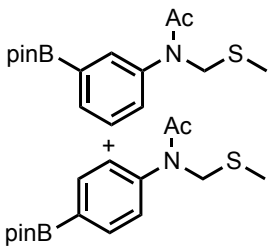
dtbpy: A mixture of *ortho*- and *meta*-borylated products (129 mg, 80% yield, *ortho* / *meta* + *para* = 2.1); *meta*-isomer (**13l**) was obtained by further purification of the crude mixture by GPC (31.0 mg, 19% yield), colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 2.24 (s, 3H), 2.63 (s, 3H), 5.21 (s, 2H), 7.57 (s, 1H), 7.63 (s, 1H), 7.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 24.8, 26.9, 72.3, 84.2, 117.6, 126.9, 128.4, 138.0, 156.8, 198.0; IR (KBr, ν/cm^{-1}) 3435, 2978, 1685, 1559, 1407, 1143, 853, 749, 664; HRMS (ESI^{+}) Calcd for $C_{16}H_{23}BO_4SNa^{+}$ ([M+Na]$^{+}$) 345.1302, Found 345.1311.

***N*-((Methythio)methyl)-*N*-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (12m).**



L9: A mixture of *ortho*-, *meta*-, and *para*-borylated products (129 mg, 80% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12m** was obtained by further purification of the crude mixture by GPC (125 mg, 78% yield), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (s, 6H), 1.31(s, 6H) 1.76 (s, 3H), 2.17 (s, 3H), 4.12 (d, *J* = 14.2 Hz, 1H), 5.44 (d, *J* = 14.2 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.37 (dd, *J* = 7.8, 6.8 Hz, 1H), 7.50 (dd, *J* = 8.2, 7.8 Hz, 1H), 7.86 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 22.7, 24.5, 24.9, 53.2, 84.0, 127.9, 129.9, 132.2, 137.0, 146.9, 170.7; IR (KBr, ν/cm^{-1}) 3734, 3648, 2975, 1652, 1396, 859, 660; HRMS (ESI^{+}) Calcd for $C_{16}H_{24}BNO_3SNa^{+}$ ([M+Na]$^{+}$) 344.1462, Found 344.1479.

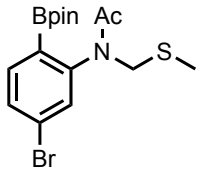
***N*-((Methylthio)methyl)-*N*-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl acetamide (13m+13m′).**



dtbpy: A mixture of *ortho*-, *meta*-, and *para*-borylated products (109 mg, 68% yield, *ortho* / *meta* + *para* = 0.5); A mixture of *meta- and para*-isomers (**13m+13m′**) was obtained by further purification by GPC (58.0 mg, 36% yield); yellow solid; *meta*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 1.84 (s, 3H), 2.14 (s, 3H), 4.83 (s, 2H), 7.33 (d, *J* = 6.9 Hz, 1H), 7.41 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.63 (s, 1H), 7.79 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 22.7, 24.8, 52.5, 84.1, 129.0, 131.5, 134.0, 134.6, 141.4,

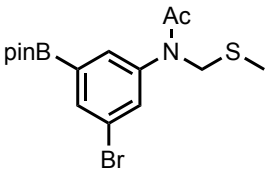
170.7; *para*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 1.86 (s, 3H), 2.13 (s, 3H), 4.83 (s, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.86 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 22.7, 24.8, 52.5, 84.1, 127.6, 136.2, 144.4, 170.5; IR (KBr, ν/cm^{-1}) 3648, 2979, 1669, 1576, 1428, 1252, 1143, 963, 867, 755, 708; HRMS (ESI^{+}) Calcd for $C_{16}H_{24}BNO_3SNa^{+}$ ([M+Na]$^{+}$) 344.1462, Found 344.1479.

***N*-(5-Bromo-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl)acetamide (12n).**



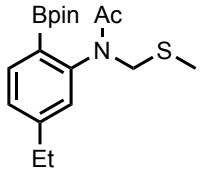
L9: A mixture of *ortho*- and *meta*-borylated products (181 mg, 91% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12n** was obtained by further purification of the crude mixture by GPC (166 mg, 83% yield); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 6H), 1.30 (s, 6H), 1.77 (s, 3H), 2.18 (s, 3H), 4.12 (d, *J* = 11.4 Hz, 1H), 5.38 (d, *J* = 11.4 Hz, 1H), 7.46 (m, 1H), 7.52-7.54 (m, 1H), 7.72 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8, 22.7, 24.5, 24.9, 53.1, 84.3, 126.0, 131.3, 133.0, 138.2, 148.1, 170.1; IR (KBr, ν/cm^{-1}) 2977, 1669, 1582, 1418, 1143, 963, 849, 766, 706; HRMS (ESI^{+}) Calcd for $C_{16}H_{23}BBrNO_3SNa^{+}$ ([M+Na]$^{+}$) 422.0567, Found 422.0559.

***N*-(3-Bromo-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl)acetamide (13n).**



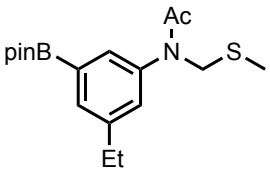
dtbpy: A mixture of *ortho*- and *meta*-borylated products (158 mg, 79% yield, *ortho* / *meta* + *para* = 0.3); *meta*-isomer (**13n**) was obtained by further purification of the crude mixture by GPC (112 mg, 56% yield); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 1.85 (s, 3H), 2.16 (s, 3H), 4.80 (s, 2H), 7.50 (s, 1H), 7.56 (s, 1H), 7.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 22.7, 24.8, 52.5, 84.5, 122.6, 132.7, 134.3, 137.4, 142.6, 170.3; IR (KBr, ν/cm^{-1}) 2977, 1669, 1418, 1143, 962, 849, 706; HRMS (ESI^{+}) Calcd for $C_{16}H_{23}BBrNO_3SNa^{+}$ ([M+Na]$^{+}$) 422.0567, Found 422.0543.

***N*-(5-Ethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl)acetamide (12o).**



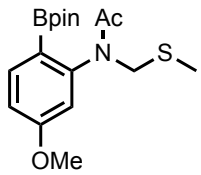
L9: A mixture of *ortho*- and *meta*-borylated products (114 mg, 65% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12o** was obtained by further purification of the crude mixture by GPC (94.0 mg, 54% yield); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (t, *J* = 7.8 Hz, 3H), 1.27 (s, 6H), 1.28 (s, 6H), 1.75 (s, 3H), 2.16 (s, 3H), 2.65 (q, *J* = 7.8 Hz, 2H), 4.11 (d, *J* = 14.2 Hz, 1H), 5.39 (d, *J* = 14.2 Hz, 1H), 7.09 (s, 1H), 7.20 (d, *J* = 7.8 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 15.7, 22.6, 24.5, 24.8, 28.7, 53.2, 83.7, 127.3, 129.2, 137.0, 147.1, 149.1, 170.6; IR (KBr, ν/cm^{-1}) 2973, 1667, 1352, 1136, 964, 855, 740, 659; HRMS (ESI$^+$) Calcd for $C_{18}H_{28}BNO_3SNa^+$ ([M+Na]$^+$) 372.1775, Found 372.1773.

***N*-(3-Ethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl)acetamide (13o).**



dtbpy: A mixture of *ortho*- and *meta*-borylated products (140 mg, 80% yield, *ortho* / *meta* + *para* = 0.5); *meta*-isomer (**13o**) was obtained by further purification of the crude mixture by GPC (88.0 mg, 50% yield); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (t, *J* = 7.8 Hz, 3H), 1.35 (s, 12H), 1.86 (s, 3H), 2.16 (s, 3H), 2.65 (q, *J* = 7.8 Hz, 2H), 4.83 (s, 2H), 7.17 (s, 1H), 7.46 (s, 1H), 7.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 15.6, 22.7, 24.8, 28.5, 52.5, 84.1, 130.9, 131.3, 134.2, 141.6, 145.4, 170.8; IR (KBr, ν/cm^{-1}) 2972, 1667, 1352, 1262, 1137, 1094, 964, 855, 740, 658; HRMS (ESI$^+$) Calcd for $C_{18}H_{28}BNO_3SNa^+$ ([M+Na]$^+$) 372.1775, Found 372.1793.

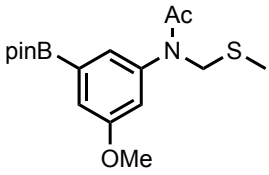
***N*-(5-Methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl) acetamide (12p).**



L9: A mixture of *ortho*- and *meta*-borylated products (128 mg, 73% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12p** was obtained by further purification of the crude mixture by GPC (120 mg, 68% yield); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 6H), 1.28 (s, 6H) 1.78 (s, 3H), 2.17 (s, 3H), 3.84 (s, 3H), 4.07 (d, *J* = 14.2 Hz, 1H), 5.42 (d, *J* = 14.2 Hz, 1H), 6.81-6.82 (m,

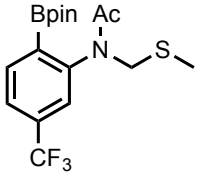
1H), 6.89 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 22.5, 24.5, 24.9, 53.1, 55.4, 83.7, 113.0, 116.0, 138.5, 148.8, 162.7, 170.5; IR (KBr, ν/cm^{-1}) 3565, 2976, 1559, 1418, 1028, 963, 857, 739, 660; HRMS (ESI$^+$) Calcd for $C_{17}H_{26}BNO_4SNa^+$ ([M+Na]$^+$) 374.1568, Found 374.1576.

***N*-(3-Methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl)acetamide (13p).**



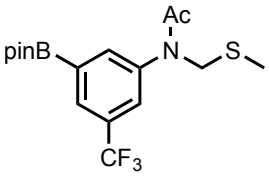
dtbpy: A mixture of *ortho*- and *meta*-borylated products (121 mg, 69% yield, *ortho* / *meta* + *para* = 0.7); *meta*-isomer (**13p**) was obtained by further purification of the crude mixture by GPC (60.0 mg, 34% yield); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 1.88 (s, 3H), 2.16 (s, 3H), 3.85 (s, 3H), 4.82 (s, 2H), 6.90 (s, 1H), 7.23 (s, 1H), 7.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 22.7, 24.8, 52.4, 55.5, 84.2, 118.3, 118.4, 126.3, 142.6, 159.9, 170.7; IR (KBr, ν/cm^{-1}) 3565, 2976, 1559, 1418, 1028, 963, 857, 739, 668; HRMS (ESI$^+$) Calcd for $C_{17}H_{26}BNO_4SNa^+$ ([M+Na]$^+$) 374.1568, Found 374.1572.

***N*-((Methylthio)methyl)-*N*-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethyl)phenyl)acetamide (12q).**



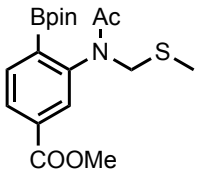
L9: A mixture of *ortho*- and *meta*-borylated products (163 mg, 84% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12q** was obtained by further purification of the crude mixture by GPC (160 mg, 82% yield); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (s, 6H), 1.32 (s, 6H), 1.76 (s, 3H), 2.18 (s, 3H), 4.16 (d, *J* = 14.2 Hz, 1H), 5.39 (d, *J* = 14.2 Hz, 1H), 7.53 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 22.8, 24.5, 24.8, 53.1, 84.5, 123.3 (q, *J* = 276 Hz), 124.4 (q, *J* = 3.8 Hz), 126.5 (q, *J* = 3.8 Hz), 133.6 (q, *J* = 33.4 Hz), 137.6, 147.3, 170.2; IR (KBr, ν/cm^{-1}) 3648, 2980, 1682, 1507, 1418, 847, 687; HRMS (ESI$^+$) Calcd for $C_{17}H_{23}BF_3NO_3SNa^+$ ([M+Na]$^+$) 412.1336, Found 412.1325.

***N*-((Methylthio)methyl)-*N*-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethyl)phenyl)acetamide (13q).**



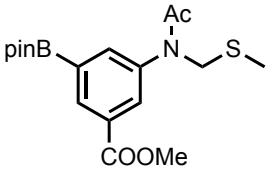
dtbpy: A mixture of *ortho*- and *meta*-borylated products (140 mg, 72% yield, *ortho* / *meta* + *para* = 0.9); *meta*-isomer (**13q**) was obtained by further purification of the crude mixture by GPC (51.0 mg, 26% yield); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 1.85 (s, 3H), 2.16 (s, 3H), 4.84 (s, 2H), 7.59 (s, 1H), 7.82 (s, 1H), 8.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 22.7, 24.4, 52.5, 84.7, 123.3 (q, J = 280 Hz), 128.1, 131.3, 131.5 (q, J = 33.3 Hz), 137.6, 141.8, 170.2; IR (KBr, ν/cm^{-1}) 3502, 2980, 1682, 1418, 964, 847, 711, 687, 623; HRMS (ESI^{+}) Calcd for $C_{17}H_{23}BF_3NO_3SNa^{+}$ ([M+Na]$^{+}$) 412.1336, Found 412.1331.

Methyl-3-(*N*-((methylthio)methyl)acetamido)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (12r).



L9: A mixture of *ortho*- and *meta*-borylated products (165 mg, 87% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12r** was obtained by further purification of the crude mixture by GPC (142 mg, 75% yield); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 6H), 1.33 (s, 6H), 1.77 (s, 3H), 2.18 (s, 3H), 3.95 (s, 3H), 4.21 (d, J = 14.2 Hz, 1H), 5.37 (d, J = 14.2 Hz, 1H), 7.90 (s, 1H), 7.93 (d, J = 7.8 Hz, 1H), 8.03 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.7, 22.8, 24.5, 24.9, 52.5, 53.1, 84.4, 128.6, 130.6, 133.7, 137.0, 146.9, 166.1, 170.4; IR (KBr, ν/cm^{-1}) 3445, 2980, 1716, 1557, 1456, 850, 705, 631; HRMS (ESI^{+}) Calcd for $C_{18}H_{26}BNO_5SNa^{+}$ ([M+Na]$^{+}$) 402.1517, Found 402.1505.

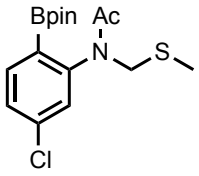
Methyl-3-(*N*-((methylthio)methyl)acetamido)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (13r).



dtbpy: A mixture of *ortho*- and *meta*-borylated products (148 mg, 78% yield, *ortho* / *meta* + *para* = 0.9); *meta*-isomer (**13r**) was obtained by further purification of the crude mixture by GPC (56.0 mg, 30% yield); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 1.82 (s, 3H), 2.14 (s, 3H), 3.91 (s, 3H), 4.82 (s, 2H), 7.80 (s, 1H), 7.96 (s, 1H), 8.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 22.7, 24.7, 52.3, 53.0, 84.3, 131.2, 132.2, 135.5, 138.5,

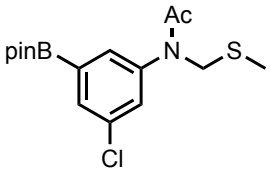
141.5, 166.0, 170.3; IR (KBr, ν/cm^{-1}) 3445, 2978, 1716, 1456, 850, 772, 705, 632; HRMS (ESI$^+$) Calcd for $C_{18}H_{26}BNO_5SNa^+$ ([M+Na]$^+$) 402.1517, Found 402.1514.

***N*-(5-Chloro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl)acetamide (12s).**



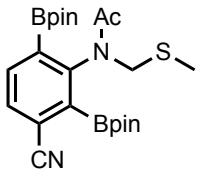
Ligand **3a**: A mixture of *ortho*- and *meta*-borylated products (115 mg, 65% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12s** was obtained by further purification of the crude mixture by GPC (106 mg, 60% yield); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 6H), 1.29 (s, 6H), 1.77 (s, 3H), 2.17 (s, 3H), 4.11 (d, *J* = 14.2 Hz, 1H), 5.39 (d, *J* = 14.2 Hz, 1H), 7.29-7.30 (m, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 22.7, 24.5, 24.9, 53.1, 84.2, 128.2, 130.1, 137.8, 138.0, 148.0, 170.2; IR (KBr, ν/cm^{-1}) 2977, 1682, 1557, 1418, 850, 669; HRMS (ESI$^+$) Calcd for $C_{16}H_{23}BClNO_3SNa^+$ ([M+Na]$^+$) 378.1072, Found 378.1057.

***N*-(3-Chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl)acetamide (13s).**



dtbpy: A mixture of *ortho*- and *meta*-borylated products (124 mg, 70% yield, *ortho* / *meta* + *para* = 0.9); *meta*-isomer (**13s**) was obtained by further purification of the crude mixture by GPC (98.0 mg, 55% yield); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 1.87 (s, 3H), 2.17 (s, 3H), 4.82 (s, 2H), 7.36 (s, 1H), 7.53 (s, 1H), 7.79 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.4, 22.8, 24.8, 52.4, 84.5, 131.5, 132.3, 134.6, 134.7, 142.5, 170.4; IR (KBr, ν/cm^{-1}) 3648, 2977, 1682, 1557, 1418, 1095, 850, 669; HRMS (ESI$^+$) Calcd for $C_{16}H_{23}BClNO_3SNa^+$ ([M+Na]$^+$) 378.1072, Found 378.1070.

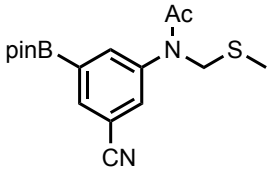
***N*-(5-Cyano-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl)acetamide (12t).**



L9: A mixture of *ortho*- and *meta*-borylated products (184 mg, 78% yield, *ortho* / *meta* + *para* = >30); *ortho*-borylated product **12t** was obtained by further purification of the crude mixture by GPC (159 mg, 67% yield); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (s, 6H), 1.33 (s, 6H), 1.36 (s,

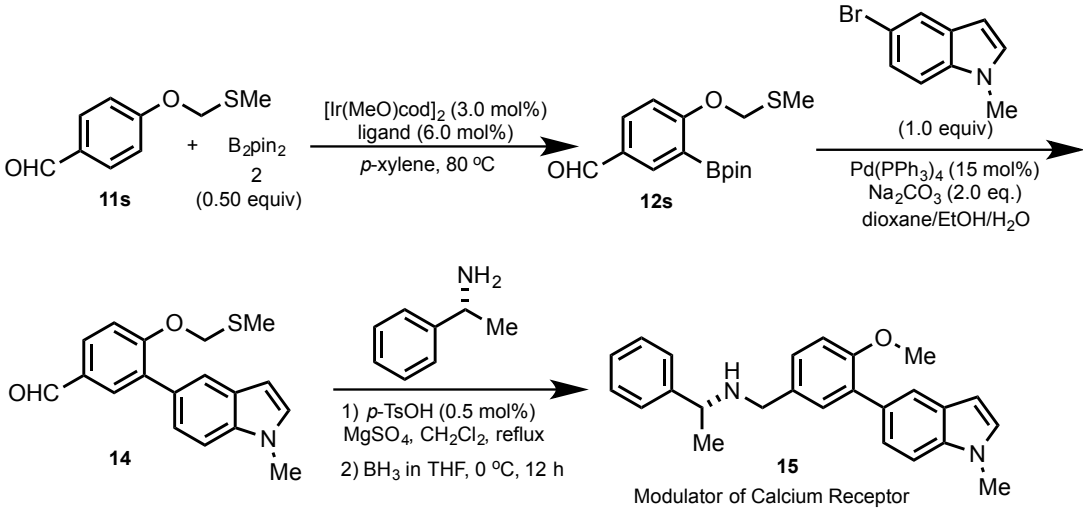
6H), 1.37 (s, 6H), 1.80 (s, 3H), 1.99 (s, 3H), 4.23 (d, J = 14.2 Hz, 1H), 5.28 (d, J = 14.2 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.4, 23.0, 24.2, 24.7, 24.8, 25.3, 54.2, 84.5, 85.4, 118.0, 119.8, 131.4, 138.1, 150.2, 170.3; IR (KBr, ν/cm^{-1}) 2977, 2227, 1668, 1329, 1132, 962, 843, 663, 607; HRMS (ESI$^+$) Calcd for $C_{23}H_{34}B_2N_2O_5SNa^+$ ([M+Na]$^+$) 495.2267, Found 495.2267.

***N*-(3-Cyano-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-*N*-((methylthio)methyl)acetamide (13t).**



dtbpy: A mixture of *ortho*- and *meta*-borylated products (114 mg, 66% yield, *ortho* / *meta* + *para* = 0.9); *meta*-isomer (**13t**) was obtained by further purification of the crude mixture by GPC (48.0 mg, 28% yield); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 1.86 (s, 3H), 2.18 (s, 3H), 4.83 (s, 2H), 7.64 (s, 1H), 7.86 (s, 1H), 8.10 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 22.8, 25.0, 52.4, 84.9, 113.5, 117.6, 134.6, 138.2, 138.6, 142.0, 170.1; IR (KBr, ν/cm^{-1}) 3446, 2980, 2226, 1666, 1543, 1313, 1132, 965, 844, 667; HRMS (ESI$^+$) Calcd for $C_{17}H_{23}BN_2O_3SNa^+$ ([M+Na]$^+$) 369.1415, Found 369.1425

Preparation of a modulator for calcium receptor.



Synthesis of compound 12s.

A mixture of 4-((methylthio)methoxy)benzaldehyde (0.500 g, 2.75 mmol), B_2pin_2 (0.350 g, 1.38 mmol), $[Ir(OMe)(cod)]_2$ (54.7 mg, 0.0825 mmol, 3.0 mol%), **L9** (49.5 mg, 0.165 mmol, 6.0 mol%), and *p*-xylene (4.5 mL) were added into a 20 mL sealed

tube and stirred at 80 ^{o}C for 24 h. The reaction mixture was concentrated under vacuum and extracted with ethyl acetate (20 mL) two times. Then, the organic layer was removed in vacu. The crude product was purified by chromatography on silica gel (hexane/ethyl acetate = 20/1) to give colorless oily product. Yield: 78%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 2.29 (s, 3H), 5.25 (s, 2H), 6.99 (d, *J* = 8.7 Hz, 1H), 7.94 (d, *J* = 8.7 Hz, 1H), 8.22 (s, 1H), 9.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 24.8, 72.2, 83.9, 113.3, 130.1, 133.5, 140.0, 166.2, 191.0; IR (KBr, ν / cm^{-1}) 3399, 2979, 1684, 1577, 1375, 850, 668; HRMS (ESI^+) Calcd for $C_{15}H_{21}BO_4SNa^+$ ($[M+Na]^+$) 331.1146, Found 331.1131.

Synthesis of compound 14.

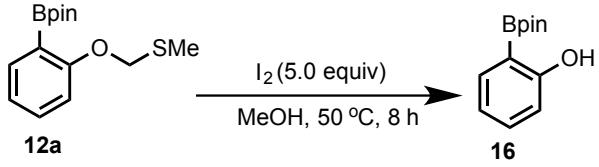
ortho-borylated compound **12s** (0.750 g, 2.44 mmol), 5-bromo-1-methyl-1*H*-indole (0.510 g, 2.44 mmol), $Pd(PPh_3)_4$ (423 mg, 0.366 mmol), and sodium carbonate (1.30 g, 12.2 mmol) were added in a 50 ml flask equipped with reflux condenser. The mixed solvents of 1,4-dioxane (8.0 mL), EtOH (5.0 mL), and water (5.0 mL) were added and the mixture was refluxed for 4 h. The reaction was cooled to room temperature and concentrated under vacuum. The mixture was extracted with EtOAc (20 mL), dried over anhydrous Na_2SO_4, and filtered. Then, the solvent was removed under vacuum and purified by column chromatography on silica gel to give a brown oil. Yield: 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14 (s, 3H), 3.83 (s, 3H), 5.20 (s, 2H), 6.52 (s, 1H), 7.09-7.10 (m, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.37-7.39 (m, 2H), 7.74-7.76 (m, 1H), 7.83 (d, *J* = 6.8 Hz, 1H), 7.90-7.95 (m, 1H), 9.96 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 32.9, 72.9, 101.3, 108.8, 114.3, 121.8, 123.2, 128.2, 128.4, 129.4, 129.8, 130.7, 133.3, 134.2, 136.1, 159.0, 191.2; IR (KBr, ν / cm^{-1}) 3648, 1698, 1598, 1507, 1215, 1159, 985; HRMS (ESI^+) Calcd for $C_{18}H_{17}NO_2SNa^+$ ($[M+Na]^+$) 334.0872, Found 334.0878.

Synthesis of modulator of calcium receptor 15.

In a 50 ml round bottom flask, compound **14** (1.20 g, 4.53 mmol), (*R*)-1-phenylethan-1-amine (0.548 g, 4.53 mmol), *p*-TsOH (3.89 mg, 0.0226 mmol) were dissolved in anhydrous CH_2Cl_2 (25 mL), then some amount of $MgSO_4$ was added in the mixture. The reaction was stirred at 50 °C for 12 h. The precipitates were filtered, and the organic layer was concentrated in vacuo to give imine intermediate.

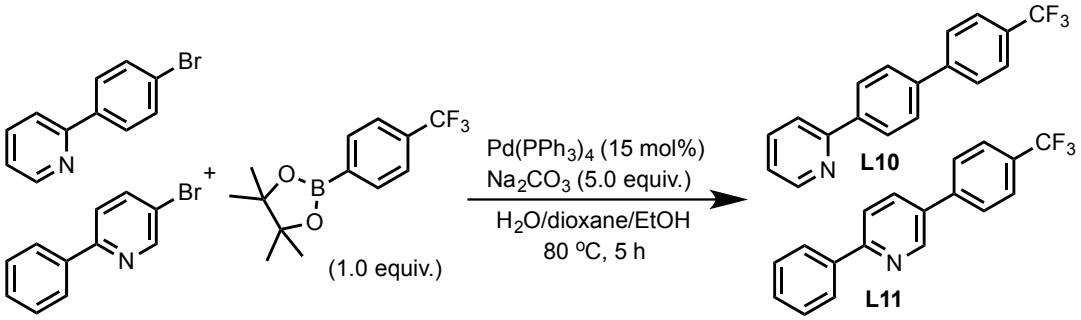
Anhydrous THF (20 mL) was used to dissolve the imine intermediate and the mixture was cooled to 0 ^{o}C. BH_3 in THF (9.06 ml, 1.0 mol/L, 2.0 equiv) was slowly dropped into the mixture. The mixture was stirred at 0 °C for 12 h. Then, the reaction mixture was concentrated in vacuo and the mixture was extracted with CH_2Cl_2 (15 mL). The organic solvent was removed in vacuo to give a crude product, which was purified by column chromatography on silica gel (hexane/ethyl acetate = 3 : 1) to give **15** as a brown oil. Yield: (1.42 g, 85%); ^{1}H NMR (400 MHz, acetone-d_6) δ 1.30 (d, J = 5.0 Hz, 3H), 3.53 (d, J = 10.5 Hz, 1H), 3.60 (d, J = 10.5 Hz, 3H), 3.76 (s, 3H), 3.82-3.84 (m, 1H), 3.85 (s, 3H), 6.44-6.45 (m, 1H), 6.99 (d, J = 6.9 Hz, 1H), 7.19-7.23 (m, 3H), 7.29-7.34 (m, 4H), 7.38-7.42 (m, 3H), 7.67 (s, 1H), 8.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 32.6, 51.0, 55.5, 57.3, 101.3, 108.4, 111.0, 121.6, 123.4, 126.6, 126.7, 127.3, 128.2, 128.3, 128.9, 129.5, 131.1, 131.8, 132.7, 135.7, 145.5, 155.5; IR (KBr, ν / cm^{-1}) 2958, 1733, 1604, 1487, 1244, 1026, 883, 757; HRMS (ESI^+) Calcd for $C_{25}H_{26}N_2ONa^+$ ([M+Na]$^+$) 393.1937, Found 393.1938.

Deprotection reaction



The *ortho*-borylated product **12a** (0.50 g, 1.79 mmol) and I_2 (0.45g, 2.0 equiv) was dissolved in MeOH and the reaction proceeded at 55 ^{o}C for 12 h. Deprotection product **16** was obtained in 83% yield. colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 6.87-6.90 (m, 2H), 7.36 (t, J = 7.3, 8.7 Hz, 1H), 7.60 (d, J = 7.7 Hz, 1H), 7.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 84.4, 115.4, 119.5, 133.8, 135.7, 163.6.

Synthesis of control ligands L10 and L11 .



Into a 30 mL two-necked flask quipped with a reflux condenser, substituted pyridine (1.00 g, 4.29 mmol), 4,4,5,5-tetramethyl-2-(4-trifluoromethyl)phenyl-1,3,2-dioxaborolane (1.12 g, 4.29 mmol, 1.0 equiv.), $Pd(PPh_3)_4$ (745 mg, 0.640 mmol), and sodium carbonate (2.30 g, 21.5 mmol) were added. After addition of 1,4-dioxane (20 mL), EtOH (12 mL), and water (12 mL), the mixture was refluxed for 4 h. The reaction was cooled to room temperature and extracted with EtOAc (20 mL) two times. The organic phase was separated and washed with H_2O (30 mL), and dried over anhydrous Na_2SO_4. The mixture was filtered, and the solvent was removed under vacuum, and the mixture purified by column chromatography on silica gel. ligand **L10**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.27 (m, 1H), 7.71-7.79 (m, 8H), 8.10 (d, *J* = 8.7, 2H), 8.72-8.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.5, 121.5 (q, *J* = 283 Hz)122.4, 125.7 (q, *J* = 38.2 Hz), 127.3, 127.5, 127.6, 129.1 (q, *J* = 31.5 Hz), 136.8, 139.2, 140.1, 144.0, 149.8, 156.7; **L11**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.47 (m, 3H), 7.51-7.53 (m, 4H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.96-7.98 (m, 1H), 8.05-8.07 (m, 2H), 8.93-8.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.5, 122.7, 125.5, 126.0 (q, *J* = 38.1 Hz), 126.9, 127.3, 128.9, 129.3, 129.9 (q, *J* = 33.3 Hz), 133.5, 135.3, 139.9 (q, *J* = 254 Hz), 148.1, 157.1; IR (KBr, ν/cm^{-1}) 3648, 2979, 1669, 1576, 1428, 1252, 1143, 963, 867, 755, 708; HRMS (ESI$^+$) Calcd for $C_{16}H_{24}BNO_3SNa^+$ ([M+Na]$^+$) 344.1462, Found 344.1479.

Publication List

[1] Hongliang Li, Yoichiro Kuninobu, Motomu Kanai, Lewis Acid-Base Interaction-Controlled *ortho*-Selective C-H Borylation of Aryl Sulfides *Angew. Chem. Int. Ed.* **2017**, *56*, 1495.

[2] Hongliang Li, Yoichiro Kuninobu, Motomu Kanai, Iridium/Bipyridine Catalyzed ortho-Selective C-H Borylation of Phenol and Aniline derivatives (*in preparation*)

Acknowledgements

The work described in this thesis would not have been possible without the help, the cooperations and support of many people, to whom I am deeply indebted.

First and foremost, I would like to express my sincere gratitude to my supervior Professor Dr. Motomu Kanai for his supreme guidance for my research activities at the University of Tokyo. His enthusiasm and his intelligence toward organic chemistry impress me so much that all these will defininately influence me in the future. As an ambitious and famous organic chemist, he kindly provided me such a precious opportunity to work in his group, which is a great honor for me forever.

Secondly, I deeply appreciate associate Professor Dr. Yoichiro Kuninobu for his excellent daily supervision and kind care during 3 year of my Ph. D. course study. He has a tremendous energy and excitement for new chemistry, and it's always inspiring to be around him. It's beyond words to describe how many important skills and knowledge I have learned from him through all od our disscusions. His nice personality and great characters would also impress me forever.

Thirdly, I gratefully acknowledge other staffs in current organic synthetic lab: Assitant Lecturer Dr. Kounosuke Oisaki, Leturer Dr. Yohei Sohma, Assistant Professor Dr. Yohei Shimizu and Assistant Professor Dr. Kenzo Yamatsugu for their frutiful suggestions and kind help in many affairs. Mrs. Sayuri Moroo, the secretary in our lab, is acknowledged for her help in daily routines at lab.

I would like to thank Leture Mrs Mikiko Kikuchi, the supervisor of the International Student Advising Room in Department of Pharmaceutical Sciences, is also thanked for her many enthusiastic helps and kind care during my stay in Japan.

I would like to thank Mrs Haruka Ida and Mitsumi Nishi for giving me losts of help to finish my research project smoothly. Without their help, I could not accomplish my research project.

I would like to collectively thank all the members in Organic Sythetic Lab for making our labortory a great working environment. There are also a number of people whom I would like to acknowledge individually: Dr. Shi-Liang Shi, Dr. Hai-Yan Zhu, Dr. Ji-Zhi Ni, Dr. Xiao-Feng Wei, Dr. Jia-An Liu, and Mr Zi-Jia Wang for helps in both life and research and many kind friends including Masahiro Nagase, Shunsuke Sueki, Mitsumi Nishi, Haruka Ida, Takahiro Shirai, Takayuki Wakai, Kenta Saito, Hideya Ikemoto, Takushi Araya, Nozomu Nagashima, Kenji Domon, Ryuto Kino, Takumi Matsueda and Kuniko Saiki.

I would also like to thank the Japanese Government (Monbukagakusho: MEXT) Scholarship for generous financial supports.

At last, I would like to express my sincere gratitude to my parents, my wife (Fangfang Xie), my sister and my brother in law for their endless supports and encouragements thoughout my overseas study and life.