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Amide directed iridium C(sp^3)–H borylation catalysis with high *N*-methyl selectivity

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ABSTRACT

A bidentate monoanionic ligand system was developed to enable iridium catalyzed C(sp^3)–H activation borylation of *N*-methyl amides. Borylated amides were obtained in moderate to good isolated yields, and exclusive mono-borylation allowed the amide to be the limiting reagent. Selectivity for C(sp^3)–H activation was demonstrated in the presence of sterically available C(sp^3)–H bonds. Competitive kinetic isotope studies revealed a large primary isotope effect, implicating C–H activation as the rate limiting step.

1. Introduction

Alkylboronic acids and esters are an important class of compounds both for the versatile reactivity of the C–B intermediate [1–5] and for inherent biological activity [6–11]. Traditionally, alkylboronic compounds are prepared by trapping alkylmagnesium [12,13] or alkyllithium [14,15] reagents with boron electrophiles. While these classical routes have low functional group tolerance, more recent transition metal based methods such as alkene or enone hydroboration [16–18], addition across C-heteroatom double bonds [19–21], and Miyaura-type borylations [22,23] largely overcome this issue [24]. However, each of these methods require the starting organic material to be prefunctionalized in preparation for the C–B bond forming reaction. This is where C–H activation has a distinct advantage. Not only is C–H activation atom efficient, it also requires little preparation of the starting organics. To this end, it has been demonstrated that Co [25], Ru [26,27], Rh [28–32], Pd [33,34], W [35], Re [36], and Ir [37–41] are capable of C(sp^3)–H activation borylation [42]. While recent advances in palladium [43–46] and cobalt [47,48] catalyzed borylations have shown exciting reactivity, the iridium based catalysts are by far the most extensively studied [42,49–53].

Pioneering work by Sawamura and co-workers with solid-supported phosphine ligands offers a directing strategy where presumably a coordinatively unsaturated metal center can accept donor directing groups. This was demonstrated in both iridium catalyzed C–H borylation (CHB) of 2-alkylpyridines with Si-SMAP ligands [54], and amide directed rhodium catalyzed CHB with an analogous immobilized phosphine ligand, Si-TRIP (Scheme 1) [31]. While this ligand generates highly active borylation catalysts, the method is limited in that the ligand synthesis requires multiple steps along with specialized silica [55] and the amide starting material is used in excess, which may be undesirable in late-stage applications. More recently, the Sawamura group developed a binol based monophosphite ligand that generates catalysts capable of enantioselective C(sp^3)–H activation. Iridium based catalysts were shown to be directed by pyridine [56], amide and ester [57] directing groups with excess substrate. Rhodium based catalysts were directed by both azines and amide functionality [58].

The Clark group demonstrated the first amide directed C(sp^3)–H borylation with a homogeneous iridium catalyst [59] using previously reported bidentate-monoanionic ligand **L2** (see Table 1) [60]. Since this initial communication, the Xu group has demonstrated a

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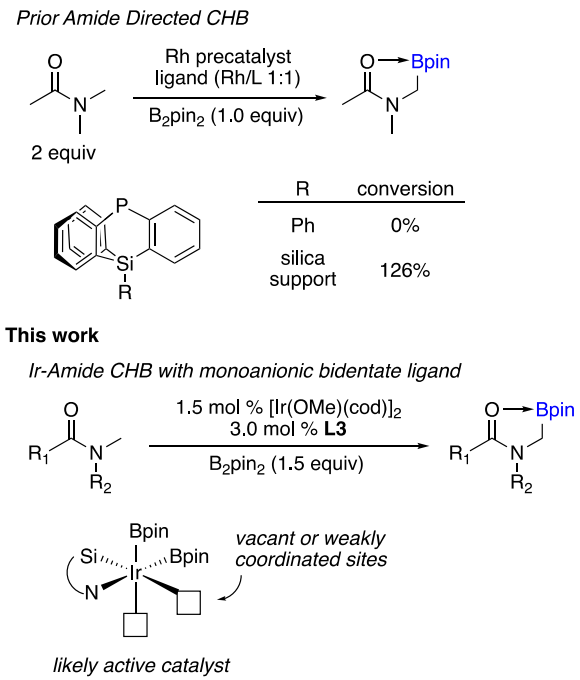


Scheme 1. Select prior amide borylation and this work.

beautiful enantioselective amide directed CHB [61–64]. While the simplicity of the ligand synthesis in Clark's system offers an advantage, the substrate scope was limited to four successful borylations (**2a**, **2d**, **2o**, **2l**, see Table 2). Furthermore, the capricious nature of the catalysts significantly limits utility. For example, the borylation of *N,N*-dimethylacetamide (**1a**) provided high conversion with moderate isolated yield (63%), while *N,N*-dimethylpentanamide (**1f**) yielded low conversion with no isolated product. With this in mind, we sought to determine if a modified bidentate-monoanionic ligands could produce catalysts capable of amide directed C(sp^3)–H borylation with increased substrate tolerance.

2. Results and discussion

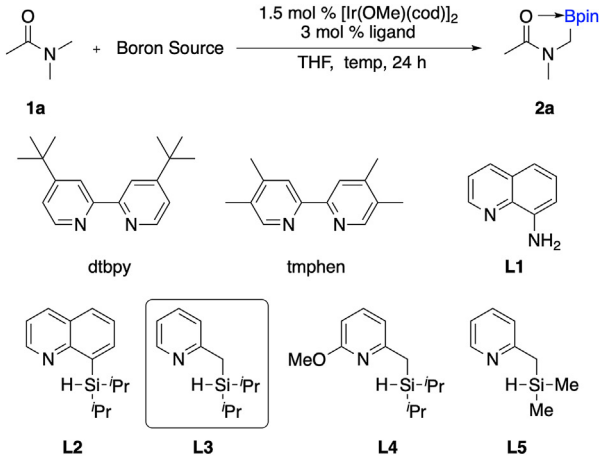
We initiated our study with the borylation of *N,N*-dimethylacetamide (**1a**) under various conditions (Table 1). As it has been shown that sp^3 CHB can occur without addition of ligand [65], and both dtbpy and tmphen (dtbpy = 4,4′-*tert*-butyl-2,2′-bipyridine, tmphen = 3,4,7,8-tetramethyl-1,10-phenanthroline) are common CHB ligands, we started by screening these conditions. No reaction occurred without ligand added and both dtbpy and tmphen provided a complex mixture of products in the ^{1}H NMR spectrum (Table 1, entries 1–3). Ligand **L1**, which has been used for ortho-selective borylations of arylimines [66], provided low conversion of **1**. Unfortunately, increased reaction temperature provided no additional conversion (entry 5). Given the low reactivity of **L1** and that Sawamura demonstrated immobilization of the phosphine ligand was necessary for the C(sp^3)–H activation to occur [31], we expected that a covalent bond between the ligand and the pre-catalyst would be crucial for generating a catalyst with the proper geometry for directed CHB. In 2014, we published silyl phosphorus and nitrogen based bidentate, monoanionic ligand frameworks for iridium catalyzed ortho selective borylations [60]. The anionic silyl ligand replaces a spectating boryl, and due to the bidentate nature, the metal to neutral donor ligand ratio is well controlled. Satisfyingly, previously reported silyl-nitrogen ligand **L2** provided 60% conversion of **1a** (entry 6). With this result, we sought to optimize the structure of this ligand framework. The pK_a of 2-methylpyridinium is 1.36 units higher than the pK_a of quinolinium in acetonitrile [67]. Since more electron rich ligands accelerate borylation rates, we prepared pyridine based ligand **L3**, which gave nearly full conversion to the desired product. Additional donation (**L4**) and decreasing the steric hindrance around the silyl site (**L5**) both provided inferior results (entries 8 and 9); however, by simply increasing the reaction temperature to 80 °C, full conversion to the product was achieved in 7.5 h (entry 10). Adjusting the boron source and lowering the catalyst loading all had a negative impact on the reaction. Solvent optimization revealed ethereal solvents provided superior conversion. Non-polar solvents such as hexane, cyclohexane, and toluene provided 75%–86% conversion while dioxane provided full conversion (see SI for details). With optimum reaction conditions in hand, we sought to explore substrate scope.

We first selected a number of acyclic and cyclic alkyl dimethyl amides (**1a-l**). Notably, perfect *N*-methyl regioselectivity was observed for compounds (**1b**) and (**1c**) where two primary C(sp^3)–H bonds are equidistant from the directing carbonyl and could potentially be activated. The increased sterics of the isopropyl group in **1c** had no adverse effect on the reaction. Moreover, increased chain length and acyclic alkyls (**1d-i**) were well tolerated. Cyclic amides (**1j-l**) proceeded smoothly; however, the reactivity of (**1j**) was significantly attenuated. We attribute the low reactivity to the increased distance of the *N*-methyl C–H bond from the directing carbonyl in the 5-membered ring (2.414 Å, calculated at ωB97x-D 6-31G*) compared to the 6- and 7-membered rings (2.243 Å and 2.241 Å respectively). Where both primary and secondary C–H bonds are available, the catalyst displays high regioselectivity for the sterically least hindered C–H bond (**1m**). While compound (**1m**) showed high selectivity for primary methyl C–H bonds, in cases with only secondary C–H bonds no reaction occurs (**1r**).

Other amide-like moieties such as a carbamate and urea directed the C(sp^3)–H borylation (**1n-o**). Product (**2n**) is a promising result as carbamates can be readily generated from the corresponding amines using standard protecting group protocols [68]. Since iridium based borylation catalysts are notably active toward C(sp^2)–H bonds, we wondered at regioselectivity of *N,N*-dimethylbenzamide (**1p**). Interestingly, the C(sp^2)–H borylation was significantly favored and no C(sp^3)–H activation was observed. Interestingly, increasing the distance between the directing amide and the C(sp^2)–H bonds by two methylene linkers yielded perfect selectivity for the C(sp^3)–H bond (**2q**). This important result demonstrates the tolerance of aromatic C–H bonds.

There were also a number of instructive substrates with no observed reactivity. Trifluoromethyl and chloro-substituted compounds (**1s-1u**) showed little to no evidence of borylation. We hypothesized that this could be due to 1) a weaker interaction between the carbonyl oxygen and iridium vacant site prohibiting the directing effect or 2) substrates **1s**-**1u** poison the catalyst. To test these ideas, we performed two borylations of **1a** in the presence of **1s** and **1t**, respectively. For the experiment with **1s**, a 60% conversion of **1a** to **2a** was observed. This shows that the fluorinated substrate **1s** is not borylated when an active borylation catalyst is present, but **1s** does impede borylation. Substrate **1a** was not borylated in the presence of **1t**, which indicates **1t** completely inhibits CHB. The cause of this inhibition is unclear, but it is noteworthy that B_2pin_2 is present at the conclusion of both reactions. Yao and co-workers recently reported Ru-catalyzed CHBs with B_2pin_2 in neat amide (1 equiv) at 120 °C [27]. Using these conditions, we attempted CHBs of substrates **1a**, **1c**, **1f** and **1o**, but no borylation occurred (see SI for details).

Table 1
Optimization of amide directed CHB.



entry	ligand	temp °C	boron source	2a[a]
1	no ligand	60	B_2pin_2	0%
2	dtbpy	60	B_2pin_2	complex mixture
3	tmphen	60	B_2pin_2	complex mixture
4	**L1**	60	B_2pin_2	10%
5	**L1**	80	B_2pin_2	10%
6	**L2**	60	B_2pin_2	60%
7	**L3**	60	B_2pin_2	91%
8	**L4**	60	B_2pin_2	complex mixture
9	**L5**	60	B_2pin_2	11%
10[b]	**L3**	80	B_2pin_2	100%
11[c]	**L3**	80	HBpin	complex mixture
12	**L3**	80	B_2eg_2	0%
13[d]	**L3**	80	B_2pin_2	85%

Conditions: Amide **1a** (1 equiv, 0.5 mmol), Boron source (1.2 equiv, 0.6 mmol), $[Ir(OMe)(cod)]_2$ (1.5 mol %, 0.0075 mmol), ligand (3 mol %, 0.015 mmol) in 2 mL THF. [a]Based on ^1H NMR. [b]Reaction time 7.5 h. [c]2 equiv HBpin. [d]0.75 mol % $[Ir(OMe)(cod)]_2$, 1.5 mol % **L3**. pin = pinacolate, eg = ethylene glycolate

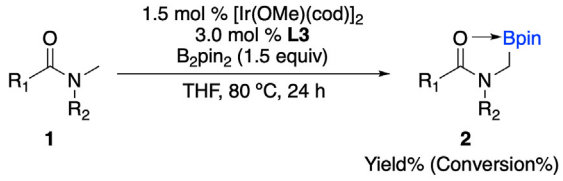
We were curious if increasing the reaction temperature would increase the reaction conversion in substrates with low conversion. For substrates **1j** and **1s**, borylation at 100 °C was conducted. No change in conversion was observed for substrate **1s**. In the case of **1j**, conversion increased from 23% to 55%. Interestingly, this higher conversion also revealed small percentages of diborylation.

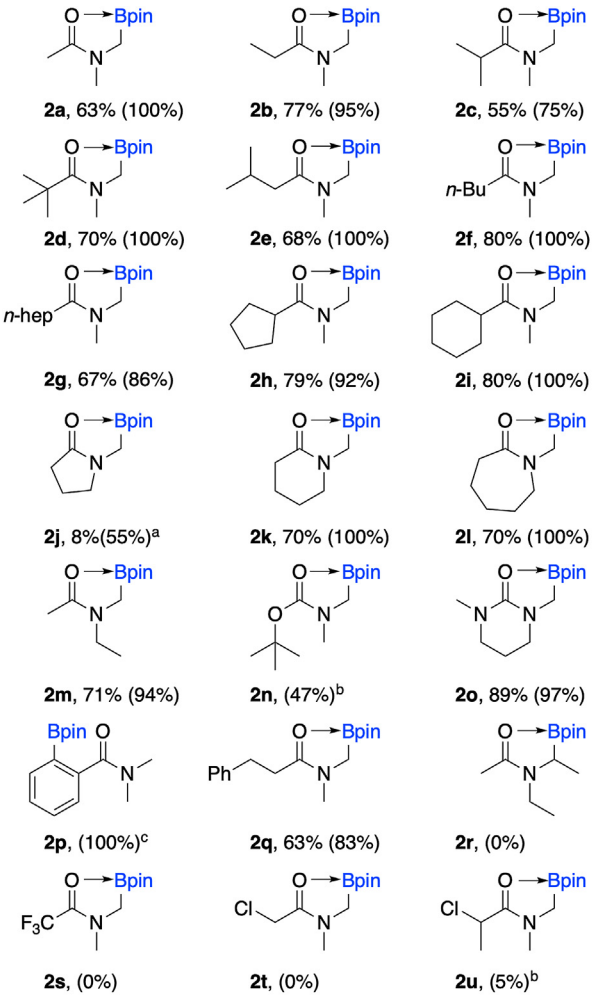
One noteworthy feature of these borylations is the difference between conversion and isolated yield. We found that the borylated products decomposed significantly when exposed to standard silica flash purification techniques. Initially, we attempted neutral alumina to isolate **2a** as Sawamura has reported successful isolation with these conditions of similar substrates [58]; however, in our hands, only 39% isolated yield was observed. One method to mitigate the decomposition on silica was to deactivate the silica by adding deionized water to the gel (35% w/w) prior to packing the silica column. Deactivation of the silica with water presumably decreases the adsorption capacity of the silica and has been shown to increase isolated yields of borylated products previously [59,69,70]. We would note that silica isolation may not be necessary depending on a user's desired follow-up chemistry as the only byproducts observed from these reactions are borates from the excess boron source.

Typically, C—H activation is the turnover-limiting step for Ir-catalyzed aromatic C—H borylations, substantiated by primary kinetic isotope effects (KIEs) where k_H/k_D values range from 3 to 5 [71]. Reported primary KIEs for Ir-catalyzed C(sp^3)—H borylations are typically lower, with k_H/k_D values ranging from 2 to 3 [38,72,73]. In our system, a competitive kinetic isotope study between *N,N*-dimethylacetamide (**1a**) and *N,N*-dimethylacetamide-d_6 (**1a-**d_6) with limiting B_2pin_2 was conducted (Scheme 2). The k_H/k_D value of 5.0 is the largest primary KIE value reported for a C(sp^3)—H borylation. Thus, C—H cleavage is the turnover limiting step.

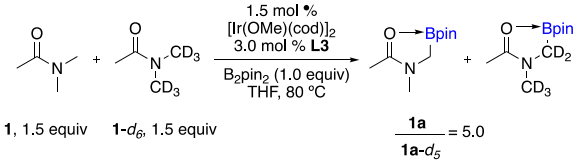
A proposed mechanism for amide borylation is presented in Scheme 3. Upon mixing the iridum precatalyst, ligand **L3** and B_2pin_2 complex **I** is generated. This 14-electron complex can readily coordinate amide substrate **1** generating 16-electron complex **II**. This initial coordination event explains the lack of reactivity observed in electron deficient substrates as they will only weakly coordinate. Complex **II** then proceeds through the turnover limiting step activating the amide *N*-methyl C(sp^3)—H bond generating complex **III**. This intermediate must then reductively eliminate the C-B bond and lose the product from the coordination sphere. The loss of product from the coordination sphere is likely assisted by a strong interaction between the carbonyl oxygen and boron in the boronic ester. This interaction is supported by a sharp boron peak in the ^{11}B NMR observed for all C(sp^3) borylated products (see SI for details). Finally, regeneration of complex **I** from complex **IV** can occur through oxidative addition of B_2pin_2 followed by reductive elimination of HBpin.

Table 2
Substrate scope.





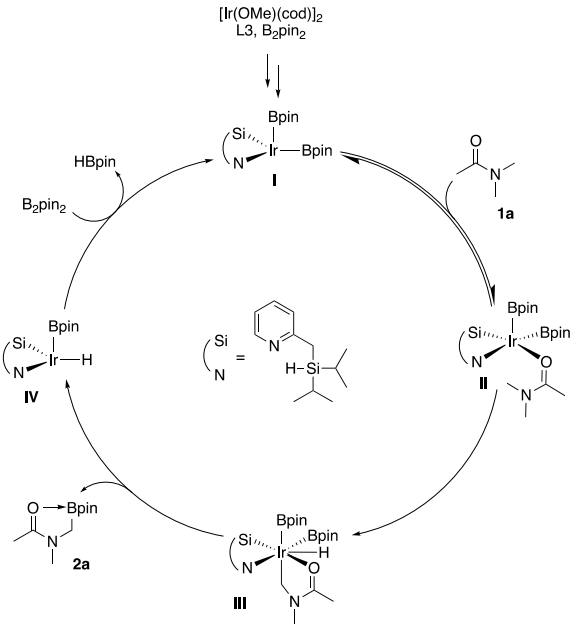
Conditions: Amide **1** (1 equiv, 1.0 mmol), B_2pin_2 (1.5 equiv, 1.5 mmol), $[Ir(OMe)(cod)]_2$ (1.5 mol %, 0.015 mmol), **L3** (3 mol %. 0.03 mmol) in 4 mL THF for 24 h.These were the conditions for all entries unless otherwise specified. [a]At 100 °C. [b]Low conversion inhibited isolation. [c]mono:diborylated 1.2:1 all $C(sp^2)$–H activation.



Scheme 2. Competitive KIE study.

3. Conclusions

A silyl-pyridine based bidentate monoanionic ligand generates a highly active homogeneous amide directed $C(sp^3)$—H borylation catalyst. Selectivity for the amide *N*-methyl C—H bond was observed. Importantly, over-borylated byproducts were not formed under these reaction conditions; thus enabling the substrate to be used as the limiting reagent unlike reported homogeneous Ru and heterogeneous Rh systems. This improvement provides potential for late stage amide directed functionalization. Other directing groups such as the urea and carbamate functional groups were



Scheme 3. Plausible catalytic cycle.

capable of C(sp^3)–H activation borylation. Importantly, C(sp^3)–H borylation occurred selectively in the presence of sp^2 C–H bonds. However, in a competitive experiment between directed sp^2 and sp^3 C–H activation, the sp^2 CHB was favored. Mechanistically, the high KIE suggests C-H activation as the rate determining step, and a catalytic cycle was proposed.

4. Experimental section

4.1. General information

All commercially available chemicals were used as received unless otherwise indicated. Bis(pinacolato)diboron (B_2pin_2) was generously supplied by BoroPharm, Inc. Bis(η^4-1,5-cyclooctadiene)-di-μ-methoxy-diiridium(I) [Ir(cod)(OMe)]$_2$ was made by a literature procedure or purchased from Sigma-Aldrich. Tetrahydrofuran (THF) was refluxed over sodium/benzophenone ketyl, distilled and degassed before use.

Column chromatography was performed on 240–400 mesh Silica P-Flash silica gel. In cases where deactivated silica gel was used, this was accomplished by adding deionized water (35% w/w) to silica gel and mixing until a non-sticky powder was observed in a round bottom flask. Thin layer chromatography was performed on 0.25 mm thick aluminum–backed silica gel plates and visualized with ultraviolet light (λ = 254 nm) and alizarin stain to visualize boronic esters. Sublimations were conducted with a water-cooled cold finger. ^{1}H, ^{13}C, ^{11}B, ^{19}F and ^{29}Si NMR spectra were recorded on a Varian 500 MHz DD2 Spectrometer equipped with a ^{1}H-^{19}F/^{15}N-^{31}P 5 mm Pulsed Field Gradient (PFG) Probe, or an Innova 300 MHz spectrometer equipped with a QUAD (^{1}H/^{19}F and ^{11}B) PFG probe. Spectra were taken in $CDCl_3$ referenced to 7.26 ppm in ^{1}H NMR and 77.0 ppm in ^{13}C NMR. Resonances for the boron-bearing carbon atom were not observed due to quadrupolar relaxation. All coupling constants are apparent J values measured at the indicated field strengths in Hertz (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublet of doublets, bs = broad singlet). NMR spectra were processed for display using the MNova software program with only phasing and baseline corrections applied. All ^{11}B NMR were collected in standard borosilicate NMR tubes. As such, a broad singlet at approximately 5 ppm can be observed in each of the spectra, which is due to the boron in the glass NMR tube. Reaction conversions were calculated by comparing the integration of the starting amide *N*-methyl peak with the borylated product methylene peak. High-resolution mass spectra (HRMS) were obtained at the Mass spectrometry analysis was performed at the Molecular Metabolism and Disease Mass Spectrometry Core facility at Michigan State University using electrospray ionization (ESI^+ or ESI^-) on quadrupole time-of-flight (Q-TOF) instruments. Melting points were measured in a capillary melting point apparatus and are uncorrected.

4.2. Ligand preparation

4.2.1. Preparation of ligand ***L2***

Ligand **L2** was prepared in similar yield following the previously reported procedure [60].

4.2.2. Preparation of ligand ***L3***

To an oven-dried 250 mL round bottom flask equipped with a stir bar, under nitrogen was added THF (40 mL) and diisopropylamine (1.1 equiv, 15.9 mmol, 2.25 mL) that was freshly distilled over calcium hydride. This solution was cooled to −78 °C in an acetone dry ice bath. Then *n*-butyllithium (2.5 M in hexanes, 1.1 equiv, 15.9 mmol, 6.36 mL) was added dropwise. This solution was allowed to stir for 5 min after which 2-methylpyridine (1.0 equiv, 14.5 mmol, 1.43 mL) that was freshly distilled over calcium hydride was slowly added dropwise. This addition took approximately 5 min after which a reddish-orange solution was observed. In a separate oven dried 250 mL round bottom flask equipped with a stir bar, under nitrogen was added THF (20 mL) and diisopropylchlorosilane (1.0 equiv, 14.5 mmol, 2.47 mL) that was freshly distilled over calcium hydride. This solution was cooled to −78 °C in an acetone dry ice bath. The contents of the flask containing the lithiated 2-methylpyridine were then slowly cannula transferred into the second flask containing the chlorosilane. This cannula transfer took approximately 20 min. Upon completion the resulting solution was allowed to stir at −78 °C for 30 min after which an aliquot was removed, quenched with methanol, and GCMS was collected. The GCMS revealed two products in a 9:1 ratio with masses corresponding to the desired monosilylated product and undesired disilylated product. The entire reaction mixture was then quenched by the addition of methanol (5 mL), solvents were removed under reduced pressure and a DCM/H_2O extraction was performed. The resulting material was further purified by distillation (oil bath temperature: 60–80 °C; vacuum: 0.01 torr). This provided **L3** as a clear colorless liquid in 58% yield (1.743 g). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 8.42 (d, J = 4.9 Hz, 1H), 7.48 (td, J = 7.7, 1.9 Hz, 1H), 7.05 (d, J = 7.9 Hz, 1H), 6.96 (dd, J = 7.4, 5.0 Hz, 1H), 3.71–3.58 (s, 1H), 2.43 (d, J = 3.7 Hz, 2H), 0.99 (s, 14H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 161.5, 149.1, 135.9, 122.6, 119.4, 22.1, 18.7, 18.6, 10.6. ^{29}Si NMR (99 MHz, $CDCl_3$): δ_{Si} 7.32.

4.2.3. Preparation of ligand ***L4***

To an oven dried 250 mL round bottom flask equipped with a stir bar, under nitrogen was added THF (50 mL) and diisopropylamine (1.1 equiv, 9.2 mmol, 1.3 mL) that was freshly distilled over calcium hydride. This solution was cooled to −78 °C in an acetone dry ice bath. Then *n*-butyllithium (2.5 M in hexanes, 1.1 equiv, 9.2 mmol, 3.7 mL) was added dropwise. This solution was allowed to stir for 10 min after which 2-methoxy-6-methylpyridine (1.0 equiv, 8.4 mmol, 1.02 mL) that was placed over 4 Å molecular sieves 24 h before use was slowly added dropwise. This addition took approximately 5 min after which an orange-yellow solution was

observed. The solution was allowed to stir for 30 min after which diisopropylchlorosilane (1.0 equiv, 8.4 mmol, 1.4 mL) freshly distilled over calcium hydride was added. This mixture stirred for 1 h then quenched by the addition of methanol (5 mL). Solvents were removed under reduced pressure and a DCM/H_2O extraction was performed. The resulting material was further purified by a silica column with a DCM/hexanes (1:9) solvent system. This provided **L4** as a clear colorless liquid in 38% yield (0.754 g). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.38 (t, $J = 7.4$ Hz, 1H), 6.63 (d, $J = 7.2$ Hz, 1H), 6.43 (d, $J = 8.1$ Hz, 1H), 3.88 (s, 3H), 3.59 (bs, 1H), 2.34 (d, $J = 3.2$ Hz, 2H), 1.02 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 163.3, 159.3, 138.5, 114.9, 105.6, 53.1, 21.5, 18.8, 18.6, 10.7. ^{29}Si NMR (99 MHz, $CDCl_3$): δ_{Si} 7.04.

4.2.4. Preparation of ligand **L5**

To an oven dried 250 mL round bottom flask equipped with a stir bar, under nitrogen was added THF (50 mL) and diisopropylamine (1.1 equiv, 14.5 mmol, 2.05 mL) that was freshly distilled from calcium hydride. This solution was cooled to −78 °C in an acetone dry ice bath. Then *n*-butyllithium (2.5 M in hexanes, 1.1 equiv, 14.5 mmol, 5.8 mL) was added dropwise. This solution was allowed to stir for 10 min after which 2-methylpyridine (1.0 equiv, 13.1 mmol, 1.3 mL)]that was freshly distilled over calcium hydride was slowly added dropwise. This addition took approximately 5 min after which a bright red-orange solution was observed. In a separate oven dried 250 mL round bottom flask equipped with a stir bar, under nitrogen was added THF (20 mL) and dimethylchlorosilane (1.0 equiv, 13.1 mmol, 1.46 mL) that was freshly distilled over calcium hydride. This solution was cooled to −78 °C in an acetone dry ice bath. The contents of the flask containing the lithiated 2-methylpyridine were then slowly cannula transferred into the second flask containing the chlorosilane. This cannula transfer took approximately 20 min. Upon completion the resulting solution was allowed to stir at −78 °C for 30 min after that the reaction was quenched by addition of silica. The silica was then rinsed with THF (250 mL) then volatiles were removed under reduced pressure. The oil was dissolved in DCM, and the solution was washed with H_2O. The organic phase was dried over $MgSO_4$, filtered, and the solvent was removed in vacuo. The ^{1}H NMR at this point showed 95% conversion of the starting material. Unusually, at ambient temperature over a week the product slowly converted back into the starting pyridine. To remove the starting materials and silicon byproducts, the compound was distilled twice with a short-path distillation head (oil bath temperature: 60–80 °C; vacuum: 0.01 torr). This provided **L5** as a clear colorless liquid in 22% yield (0.436 g) that matched previously reported spectra [74]. Unfortunately, this purified compound also slowly decomposed in a nitrogen filled glove box at ambient temperature.

^{1}H NMR (500 MHz, $CDCl_3$): δ_H 8.44 (d, $J = 5.0$ Hz, 1H), 7.51 (td, $J = 7.7, 1.9$ Hz, 1H), 7.04–6.93 (m, 2H), 4.02 (m, $J = 3.6$ Hz, 1H), 2.42 (d, $J = 3.6$ Hz, 2H), 0.10 (d, $J = 3.6$ Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 160.9, 149.2, 136.0, 122.3, 119.4, 27.6, −4.5.

4.2.5. General borylation procedure

In a nitrogen-filled glove box, $[Ir(OMe)(cod)]_2$, the desired ligand, and B_2pin_2 were weighed into separate test tubes, and the starting amide was weighed into a 5 mL conical vial equipped with a stir bar. To the test tube containing $[Ir(OMe)(cod)]_2$ was added ~0.2 mL THF. The resulting solution was then transferred into the test tube containing B_2pin_2. The contents of the first test tube were rinsed three times (~0.2 mL/rinse) and added to the test tube containing B_2pin_2. The solution of $[Ir(OMe)(cod)]_2$ and B_2pin_2 was then transferred into the test tube containing the ligand by a similar rinsing procedure described above. Finally, the resulting solution was added to the 5 mL conical vial followed by the rinsing procedure. The conical vial was then sealed and placed in an aluminum block pre-heated to the desired temperature and allowed to stir for the desired time. The vial was then opened, solvent was removed via rotary evaporation, and a ^{1}H NMR spectrum of the crude material was recorded. The crude reaction mixture was passed through deactivated silica (35% H_2O w/w) with a gradient solvent system of 10%–15% MeOH in EtOAc. The product was then collected and dried overnight under high vacuum prior to collecting the reported analytical data.

Table 1 Entry 1:

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv) and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 60 °C and allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. Only starting material was observed.

Table 1 Entry 2:

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), dtbpy (4.0 mg, 0.015 mmol, 3 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 60 °C and allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. A complex mixture of products was observed.

Table 1 Entry 3:

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), tmphen (3.5 mg, 0.015 mmol, 3 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 60 °C and allowed to stir for 24 h.The ^{1}H NMR spectrum of the crude material was recorded. A complex mixture of products was observed.

Table 1 Entry 4:

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), **L1** (2.2 mg, 0.015 mmol, 3 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 60 °C and allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. A 10% conversion of starting material was observed.

Table 1 Entry 5:

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), **L1** (2.2 mg, 0.015 mmol, 3 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 60 °C and allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. A 10% conversion of starting material was observed.

Table 1 Entry 6:

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), **L2** (3.7 mg, 0.015 mmol, 3 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 60 °C and allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. A 60% conversion of starting material was observed.

Table 1 Entry 7:

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), **L3** (3.1 mg, 0.015 mmol, 3 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 60 °C and allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. A 91% conversion of starting material was observed.

Table 1 Entry 8:

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), **L4** (3.6 mg, 0.015 mmol, 3 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 60 °C and

allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. A complex mixture of products was observed.

Table 1 Entry 9:

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), **L5** (2.3 mg, 0.015 mmol, 3 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 60 °C and allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. An 11% conversion of starting material was observed.

Table 1 Entry 10:

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), **L3** (3.1 mg, 0.015 mmol, 3 mol %), B_2pin_2 (152.4 mg, 0.6 mmol, 1.2 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 80 °C and allowed to stir for 7.5 h. The ^{1}H NMR spectrum of the crude material was recorded. A 100% conversion of starting material was observed.

Table 1 Entry 11:

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), **L3** (3.1 mg, 0.015 mmol, 3 mol %), HBpin (128.0 mg, 1.0 mmol, 2.0 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 80 °C and allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. A complex mixture of products was observed.

Table 1 Entry 12:

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (4.97 mg, 0.0075 mmol, 1.5 mol %), **L3** (3.1 mg, 0.015 mmol, 3 mol %), B_2eg_2 (85.0 mg, 0.6 mmol, 1.0 equiv), and *N,N*-dimethylacetamide (43.5 mg, 0.5 mmol, 1.0 equiv) were reacted at 80 °C and allowed to stir for 24 h. The ^{1}H NMR spectrum of the crude material was recorded. Only starting material was observed.

4.3. Borylation of *N,N*-dimethylacetamide (***2a***)

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethylacetamide (1 mmol, 1.0 equiv, 87.1 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 100% conversion of starting material. After isolation, **2a** was obtained as a white solid (132.7 mg, 62% yield, mp = 116–121 °C, lit mp = 145.2–147.5 °C [31], 157.4–162.8 °C [59]) that matched previously reported spectra. ^{1}H NMR (500 MHz, $CDCl_3$) [31]: δ_H 3.07 (s, 3H), 2.40 (s, 2H), 2.14 (s, 3H), 1.19 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) [31]: δ_C 174.2, 79.8, 36.0, 25.0, 15.4. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 12.61 (s). HRMS (ESI) *m/z* calc for $C_{10}H_{20}BNO_3Na$ [(M + Na)$^+$] 236.1433, found 236.1463.

4.3.1. Borylation of *N,N*-dimethylpropionamide (***2b***)

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethylpropionamide (1 mmol, 1.0 equiv, 101.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 95% conversion of starting material. After isolation, **2b** was obtained as a white solid (174.9 mg, 77% yield, mp = 118–120 °C, lit mp = 151.1–152.7 °C [27]) that matched previously reported spectra. ^{1}H NMR (500 MHz, $CDCl_3$) [27]: δ_H 3.05 (s, 3H), 2.43–2.36 (m, 4H), 1.21 (t, J = 7.6 Hz, 3H), 1.19 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) [27]: δ_C. 177.5, 79.9, 35.5, 25.1, 22.1, 8.7. ^{11}B NMR (160 MHz, $CDCl_3$) [27]: δ_B 12.2 (s).(12.5 ppm lit) [27] HRMS (ESI) *m/z* calc for $C_{11}H_{22}BNO_3Na$ [(M + Na)$^+$] 250.1590, found 250.1953.

4.3.2. Borylation of *N,N*-dimethylisobutyramide (***2c***)

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethylisobutyramide (1 mmol, 1.0 equiv, 115.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 75% conversion of starting material. After isolation **2c** was obtained as a white solid (132.6 mg, 55% yield, mp = 81–85 °C) that matched previously reported spectra. ^{1}H NMR (500 MHz, $CDCl_3$) [27]: δ_H 3.09 (s, 3H), 2.75 (sept, J = 6.9 Hz, 1H), 2.40 (s, 2H), 1.18 (d, J = 6.0 Hz, 6H), 1.19 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) [27]: δ_C 180.2, 79.8, 35.4, 27.4, 25.1, 18.5. ^{11}B NMR (160 MHz, $CDCl_3$) [5]: δ_B 12.37 (s).(12.1 ppm lit) [27] HRMS (ESI) *m/z* calc for $C_{12}H_{24}BNO_3Na$ [(M + Na)$^+$] 264.1746, found 264.1778.

4.3.3. Borylation of *N,N*-dimethylpivalamide (***2d***)

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethylpivalamide (1 mmol, 1.0 equiv, 129.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 100% conversion of starting material. After isolation, **2d** was obtained as a white solid (178.6 mg, 70% yield, mp = 61–64 °C, lit mp = 60.8–63.9 °C [59]) that matched previously reported spectra. ^{1}H NMR (500 MHz, $CDCl_3$) [59]: δ_H 3.20 (s, 3H), 2.45 (s, 2H), 1.31 (s, 9H), 1.17 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) [59]: δ_C 181.1, 79.7, 37.6, 35.6, 27.2, 25.1. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 11.74 (s). HRMS (ESI) *m/z* calc for $C_{13}H_{26}BNO_3$ [M]$^+$ 255.2005, found 255.2099.

4.3.4. Borylation of *N,N,3*-trimethylbutanamide (***2e***)

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N,3*-trimethylbutanamide (1 mmol, 1.0 equiv, 129.20 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 100% conversion of starting material. After isolation, **2e** was obtained as a white solid (173.5 mg, 68% yield, mp = 62–65 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.06 (s, 3H), 2.25 (d, J = 7.6 Hz, 2H), 2.10 (s, 2H), 2.17 (m, 1H), 1.18 (s, 12H), 0.99 (d, J = 6.6 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 176.3, 79.7, 36.9, 35.9, 25.9, 25.1, 22.5. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 12.41 (s). HRMS (ESI) *m/z* calc for $C_{13}H_{26}BNO_3$ [M]$^+$ 255.2005, found 255.2138.

4.3.5. Borylation of *N,N*-dimethylpentanamide (***2f***)

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethylpentanamide (1 mmol, 1.0 equiv, 129.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 100% conversion of starting material. After isolation, **2f** was obtained as a white solid (202.8 mg, 80% yield, mp = 104–106 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.05 (s, 3H), 2.38 (s, 2H), 2.36 (t, J = 7.8 Hz, 2H), 1.65 (m, J = 7.8 Hz, 2H), 1.37 (m, J = 7.4 Hz, 2H), 1.18 (s, 12H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 176.9, 79.8, 35.7, 28.2, 26.6, 25.1, 22.3, 13.6. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 12.44 (s). HRMS (ESI) *m/z* calc for $C_{13}H_{26}BNO_3Na$ [(M + Na)$^+$] 278.1903, found 278.1937.

4.3.6. Borylation of *N,N*-dimethyloctanamide (***2g***)

Following the general borylation procedure [Ir(OMe)(cod)]$_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethyloctanamide (1 mmol, 1.0 equiv, 171.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 86% conversion of starting material. After isolation, **2g** was obtained as a white solid (199.1 mg, 67% yield, mp = 120–123 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.05 (s, 3H), 2.38 (s, 2H), 2.35 (t, J = 7.6 Hz, 2H), 1.66 (m, J = 7.9 Hz, 2H), 1.35–1.26 (m, 8H), 1.18 (s, 12H), 0.88 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 177.0, 79.8, 35.7, 31.5, 29.1, 28.8, 28.5, 25.2, 24.5, 22.5, 14.0. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 12.49 (s). HRMS (ESI)

m/z calc for $C_{16}H_{32}BNO_3$ $[M]^+$ 297.2475, found 297.2606.

4.3.7. Borylation of N,N-dimethylcyclopentanecarboxamide (**2h**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethylcyclopentanecarboxamide (1 mmol, 1.0 equiv, 141.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 92% conversion of starting material. After isolation, **2h** was obtained as a white solid (210.2 mg, 79% yield, mp = 98–99 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.06 (s, 3H), 2.83 (p, J = 8.0 Hz, 1H), 2.37 (s, 2H), 1.91–1.71 (m, 6H), 1.65–1.51 (m, 2H), 1.16 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 179.8, 79.7, 37.4, 35.6, 29.8, 25.9, 25.1. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 12.31 (s). HRMS (ESI) *m/z* calc for $C_{14}H_{26}BNO_3Na$ $[(M + Na)^+]$ 290.1903, found 290.1940.

4.3.8. Borylation of N,N-dimethylcyclohexanecarboxamide (**2i**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethylcyclohexanecarboxamide (1 mmol, 1.0 equiv, 155.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 100% conversion of starting material. After isolation, **2i** was obtained as a white solid (225.1 mg, 80% yield, mp = 139–140 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.07 (s, 3H), 2.44 (tt, J = 11.6, 3.5 Hz, 1H), 2.37 (s, 2H), 1.87–1.67 (m, 5H), 1.61–1.51 (m, 2H), 1.32–1.21 (m, 3H), 1.18 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 179.2, 79.7, 37.0, 35.4, 28.2, 25.3, 25.3, 25.1. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 12.38 (s). HRMS (ESI) *m/z* calc for $C_{15}H_{28}BNO_3Na$ $[(M + Na)^+]$ 304.2059, found 304.2095.

4.3.9. Borylation of 1-methylpyrrolidin-2-one (**2j**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and 1-methylpyrrolidin-2-one (1 mmol, 1.0 equiv, 99.1 mg) were reacted at 80 °C and allowed to stir for 24 h. There was a conversion of 23% based on ^{1}H NMR. When the reaction was conducted at 100 °C and allowed to stir for 24 h, 55% conversion was observed. Based on GC/MS analysis a ratio of 2.3:1 mono:di-borylation was observed. From this mixture, we were unable to isolate the diborylated compound and complete removal of B_2pin_2 and borates was challenging. By sublimation at 60 °C under high-vacuum (0.01 mm Hg), 180 mg of 8:1 mono:di-borylated was isolated. Subsequent sublimation yield 20 mg (8% yield) of the monoborylated product. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.39 (t, J = 6.3 Hz, 2H), 2.67 (s, 2H), 2.38 (t, J = 8.1 Hz, 2H), 2.04 (m, 2H), 1.27 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 175.9, 83.5, 83.4, 49.0, 29.4, 25.0, 24.9, 24.6, 18.1. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 22.27 (s).

4.3.10. Borylation of 1-methylpiperidin-2-one (**2k**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and 1-methylpiperidin-2-one (1 mmol, 1.0 equiv, 113.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 100% conversion of starting material. After isolation, **2k** was obtained as a white solid (107.1 mg, 70% yield, mp = 127–131 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.31 (t, J = 5.7 Hz, 2H), 2.49 (t, J = 6.2 Hz, 2H), 2.34 (s, 2H), 1.90–1.75 (m, 4H), 1.19 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 173.9, 79.9, 47.8, 26.4, 25.2, 22.0, 19.5. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 12.68 (s). HRMS (ESI) *m/z* calc for $C_{12}H_{22}BNO_3Na$ $[(M + Na)^+]$ 262.1590, found 262.1624.

4.3.11. Borylation of 1-methylazepan-2-one (**2l**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and 1-methylazepan-2-one (1 mmol, 1.0 equiv, 127.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 100% conversion of starting material. After isolation, **2l** was obtained as a white solid (176.6 mg, 70% yield, mp = 110–113 °C, lit mp = 118.3–120.2 °C [5],116.8–120.6 °C [4], 128.3–129.8 °C [3]) that matched previously reported spectra. ^{1}H NMR (500 MHz, $CDCl_3$) [5]: δ_H 3.45–3.34 (m, 2H), 2.61–2.52 (m, 2H), 2.49 (s, 2H), 1.77–1.68 (m, 2H), 1.67–1.60 (m, 4H), 1.15 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) [5]: δ_C 179.5, 79.8, 50.4, 31.2, 29.8, 26.3, 25.1, 22.1. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 12.52 (s).HRMS (ESI) *m/z* calc for $C_{13}H_{24}BNO_3Na$ $[(M + Na)^+]$ 276.1746, found 276.1786.

4.3.12. Borylation of N-ethyl-N-methylacetamide (**2m**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N*-ethyl-N-methylacetamide (1 mmol, 1.0 equiv, 101.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 94% conversion of starting material. After isolation, **2m** was obtained as a white solid (161.2 mg, 71% yield, mp = 149–153 °C) ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.37 (q, J = 7.3 Hz, 2H), 2.36 (s, 2H), 2.13 (s, 3H), 1.20 (t, J = 7.3 Hz, 3H), 1.17 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 173.7, 79.9, 43.7, 25.1, 15.4, 12.7. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 12.41 (s) HRMS (ESI) *m/z* calc for $C_{11}H_{22}BNO_3Na$ $[(M + Na)^+]$ 250.1590, found 250.1620.

4.3.13. Borylation of tert-butyl dimethylcarbamate (**2n**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *tert*-butyl dimethylcarbamate (1 mmol, 1.0 equiv, 145.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 47% conversion of starting material. ^{1}H NMR of crude material matched previous spectra [75]. No other byproducts were observed in the ^{1}H NMR or the GCMS of crude reaction mixture.

4.3.14. Borylation of 1,3-dimethyltetrahydropyrimidin-2(1H)-one (**2o**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and 1,3-dimethyltetrahydropyrimidin-2(1H)-one (1 mmol, 1.0 equiv, 128.2 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 100% conversion of starting material. After isolation, **2o** was obtained as a white solid (227.4 mg, 89% yield, mp = 165–167 °C, lit mp = 165.2–166.6 °C [3]) that matched previously reported spectra. ^{1}H NMR (500 MHz, $CDCl_3$) [3]: δ_H 3.34–3.14 (m, 4H), 2.98 (s, 3H), 2.34 (s, 2H), 1.96 (m, 2H), 1.18 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) [3]: δ_C 159.5, 79.6, 46.6, 44.6, 36.0, 25.2, 20.9. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 11.53 (s). HRMS (ESI) *m/z* calc for $C_{12}H_{23}BN_2O_3Na$ $[(M + Na)^+]$ 277.1699, found 277.1705.

4.3.15. Borylation of N,N-dimethylbenzamide (**2p**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethylbenzamide (1 mmol, 1.0 equiv, 149.2 mg) were reacted at 80 °C and allowed to stir for 24 h. The starting material was 100% consumed with the major product being the ortho borylated product. The spectra for **2p** was in accordance with a previous report [76]. The spectra also showed diborylated material in 1.2:1 ratio of mono:di-borylated.

4.3.16. Borylation of N,N-dimethyl-3-phenylpropanamide (**2q**)

Following the general borylation procedure $[Ir(OMe)(cod)]_2$

(0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.9 mg), and *N,N*-dimethyl-3-phenyl propanamide (1 mmol, 1.0 equiv, 177.3 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 83% conversion of starting material. After isolation, **2q** was obtained as a white solid 191.0 mg, 63% yield, mp = 98–103 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.34–7.27 (m, 2H), 7.24–7.22 (m, 1H), 7.21–7.15 (m, 2H), 3.05–2.97 (m, 2H), 2.93 (s, 3H), 2.71–2.60 (m, 2H), 2.39 (s, 2H), 1.21 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 175.8, 139.7, 128.7, 128.3, 126.6, 80.0, 35.5, 30.8, 30.6, 25.2. ^{11}B NMR (160 MHz, $CDCl_3$): δ_B 13.09 (s). HRMS (ESI) *m/z* calc for $C_{17}H_{26}BNO_3Na$ [(M + Na)$^+$] 326.1903, found 326.1956.

*4.3.17. Borylation of N,N-diethylacetamide (**2r**)*

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.0075 mmol, 1.5 mol %, 4.9 mg), **L3** (0.015 mmol, 3 mol %, 3.1 mg), B_2pin_2 (0.75 mmol, 1.5 equiv, 190.4 mg), and *N,N*-diethylacetamide (0.5 mmol, 1.0 equiv, 57.6 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 0% conversion of starting material based on ^{1}H NMR.

*4.3.18. Borylation of 2,2,2-trifluoro-N,N-dimethylacetamide (**2s**)*

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.0075 mmol, 1.5 mol %, 4.9 mg), **L3** (0.015 mmol, 3 mol %, 3.1 mg), B_2pin_2 (0.75 mmol, 1.5 equiv, 190.4 mg), and 2,2,2-trifluoro-*N,N*-dimethyl acetamide (0.5 mmol, 1.0 equiv, 70.5 mg) were reacted at 80 °C and at 100 °C and allowed to stir for 24 h. There was 0% conversion of starting material based on ^{1}H and ^{19}F NMR.

*4.3.19. Borylation of 2-chloro-N,N-dimethylacetamide (**2t**)*

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.8 mg), and 2-chloro-*N,N*-dimethyl acetamide (1.0 mmol, 1.0 equiv, 121.5 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 0% conversion of starting material based on ^{1}H NMR.

*4.3.20. Borylation of 2-chloro-N,N-dimethylpropanamide (**2u**)*

Following the general borylation procedure $[Ir(OMe)(cod)]_2$ (0.015 mmol, 1.5 mol %, 9.9 mg), **L3** (0.03 mmol, 3 mol %, 6.2 mg), B_2pin_2 (1.5 mmol, 1.5 equiv, 380.8 mg), and 2-chloro-*N,N*-dimethy lpropanamide (1.0 mmol, 1.0 equiv, 135.5 mg) were reacted at 80 °C and allowed to stir for 24 h. There was 5% conversion of starting material based on ^{1}H NMR.

Associated content

Supporting Information Available: Full characterization, copies of all spectral data, and experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

Declaration of competing interest

M.R.S. and R.E.M. own a percentage of BoroPharm, Inc.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2021.132578.

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