Phosphine-Directed sp^3 C–H, C–O, and C–N Borylation

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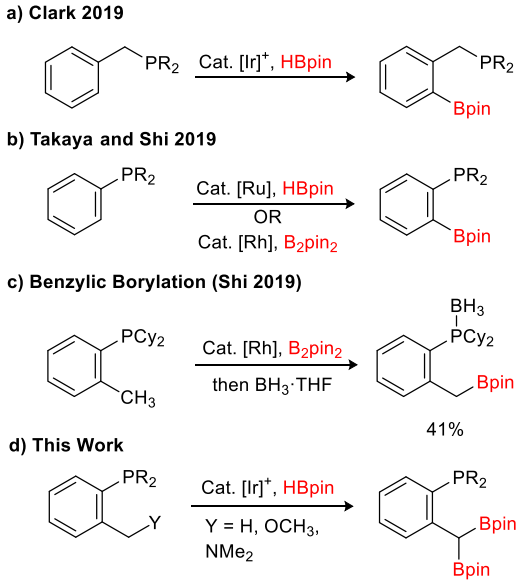
Supporting Information Placeholder

ABSTRACT: Benzylic C–H borylation reactions are limited, requiring new approaches to understand their reactivity for efficient selective functionalization. The recent development of phosphine-directed C–H borylation of arenes has now been extended to benzylic substrates, providing high yield of the mono- and geminal bis-borylation products. Attempts to borylate the C–H bond alpha to a benzylic ether or amine resulted in C–O and C–N borylation, followed by C–H borylation to provide geminal bis-borylated products.

The borylation of sp^2 and sp^3 C–H bonds has received significant attention over the past two decades, resulting in numerous robust catalysts that have been applied to a variety of substrate classes.[1-3] Early work focused on sterically-controlled regioselectivity of arenes (avoids borylation ortho to substituents) and alkanes (selects for primary C–H bonds).[4] Starting in 2008, catalyst/substrate combinations were designed that could reverse the sterically-controlled C–H borylation of arenes and direct the catalyst to the ortho position.[5-26] While this approach has been used extensively with arenes, there has been much less reported for using directing groups for regioselective alkane C–H borylation.[27-35] Among these, several examples include benzylic C–H bonds.[36-44]

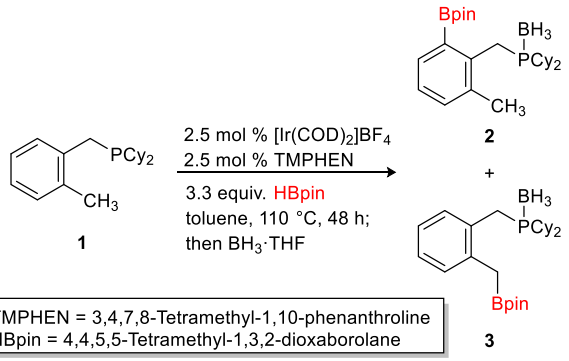
Scheme 1. Context of Phosphine-Directed C–H Borylation



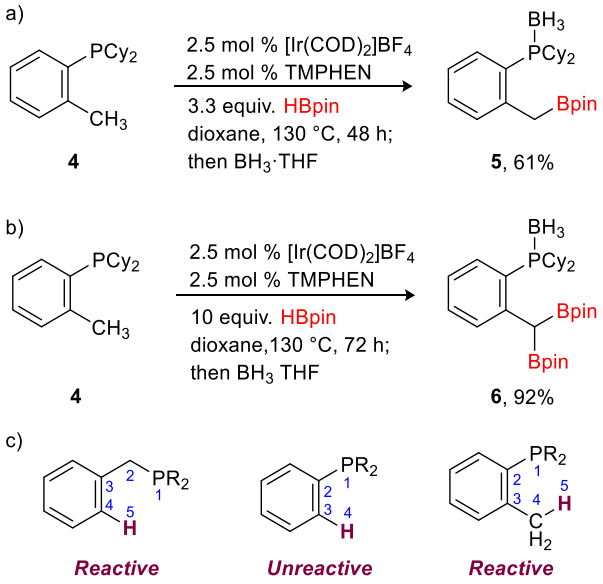
Phosphine-directed C–H borylation was initially reported by our group in 2014.[15] That initial report was extended to a more general cationic iridium catalyst in 2019 (Scheme 1a).[45] Concurrent publications by Shi[46] and Takaya[47] reported analogous phosphine-directed C–H borylation of aryl phosphines with rhodium and ruthenium catalysts, respectively (Scheme 1b). In Shi's work, one example of phosphine-directed benzylic C–H borylation was also demonstrated, providing a modest yield of the mono-borylated product (Scheme 1c). Our prior work on phosphine-directed C–H borylation suggested that a more efficient and general benzylic C–H borylation of phosphines was possible. In this report we detail the cationic iridium-catalyzed benzylic C–H borylation, which proceeds in high yields and favoring the bis-borylated products. Furthermore, the presence of a benzylic ether or amine are shown to undergo C–O and C–N borylation, respectively.

During our efforts to determine the substrate scope of the phosphine-directed C–H borylation reaction (Scheme 1a), some substrates provided a complex mixture of borylation products. Borylation of *ortho*-methylbenzyldicyclohexylphosphine (**1**, Scheme 2) provided a mixture of the expected arene borylation (**2**), as well as other borylation products that were believed to result from benzylic C–H borylation (**3**).

Scheme 2. Initial Discovery of Benzylic C–H Borylation



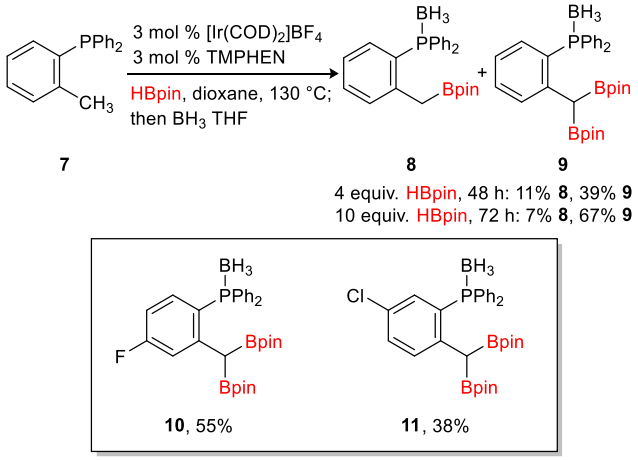
To gain more insight into the ability to provide efficient benzylic C–H borylation, dicyclohexyl(2-methylphenyl) phosphine (**4**, Scheme 3) was chosen for functionalization. From our previous work using this catalyst,[45] reactive phosphines required at least 5 atoms (from phosphorus to the functionalized hydrogen, see Scheme 3c) to afford borylation products. In the case of substrate **4**, the benzylic C–H bond is the only reactive C–H bond that meets this requirement. Using similar conditions to those previously reported, a good yield of monoborylation product **5** was obtained upon borane protection of the phosphine (Scheme 3a). Furthermore, increasing the equivalents of pinacolborane and extending the reaction time to 72 h, resulted in selective formation of bis-borylated product **6** in high yield (Scheme 3b).



Scheme 3. Benzylic C–H Borylation of Phosphine **4**

Replacing the cycylohexyl substituents of **4** with phenyl substituents, resulted in a moderate change to the reactivity. Using the conditions that favored monoborylation with **4** (Scheme 3a), borylation of **7** favored bisborylation product **9** (~1:4 **8**/**9**) in a combined 50% isolated yield (Scheme 4). Attempts to decrease the temperature or equivalents of pinacolborane resulted in low yields and still favored **9**. Increasing to 10 equivalents of pinacolborane, however, provided a 67% isolated yield of **9** with an additional 7% of **8**. Halogen-substituted versions of **7** were also examined under the reaction conditions (10 equivalents of HBpin for 72 h), providing moderate yields of the corresponding bis borylation products (**10** and **11**, Scheme 4).

Scheme 4. Benzylic C–H Borylation of Phosphine **7**



A series of readily available related phosphines were examined, but a narrow reactivity window was observed. Tri-*ortho*-tolylphosphine (**12**, Figure 1) resulted in low conversions and a mixture of mono-, bis-, and tris-borylation products. Phosphine **13**, with bis-ortho methyls, was found to be unreactive, likely due to the increased steric congestion around the directing phosphine. Finally, biaryl phosphine **14** was also unreactive under the reaction conditions.

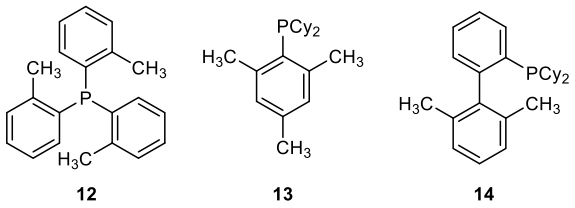
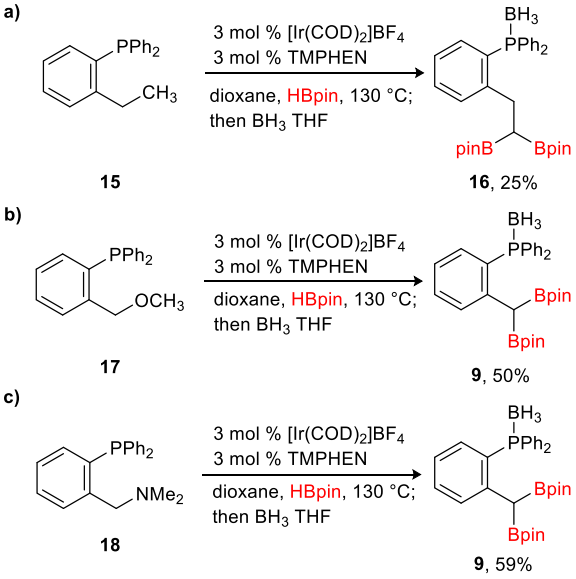


Figure 1. Unreactive or Unselective Phosphine Substrates

In spite of the limited reactivity, the ability to borylate secondary C–H bonds was enticing. To this end, three substrates were chosen to determine if secondary, benzylic C–H borylation was possible. Phosphine **15**, which has an ethyl in place of the methyl of **7**, was examined under the reaction conditions (Scheme 5a). The major borylated product from this reaction was from bisborylation of the terminal methyl rather than the benzylic position, forming **16** in a modest yield. Expecting an α-heteroatom to increase the reactivity of the benzylic C–H bond, ether **17** was then examined. To our surprise, the major product formed under the reaction conditions was bisborylation product **9**, which was isolated in 50% yield (Scheme 5b), along with an additional 10% of monoborylation product **8**. Expecting C–N borylation to be less competitive with C–H borylation, benzylic amine **18** was examined under the reaction conditions. Similar to the ether, bisborylation product **9** was the major product observed (59%), along with 8% monoborylation product **8** (Scheme 5c).

Scheme 5. Attempted Secondary C–H Borylation Resulting in C–O and C–N Borylation

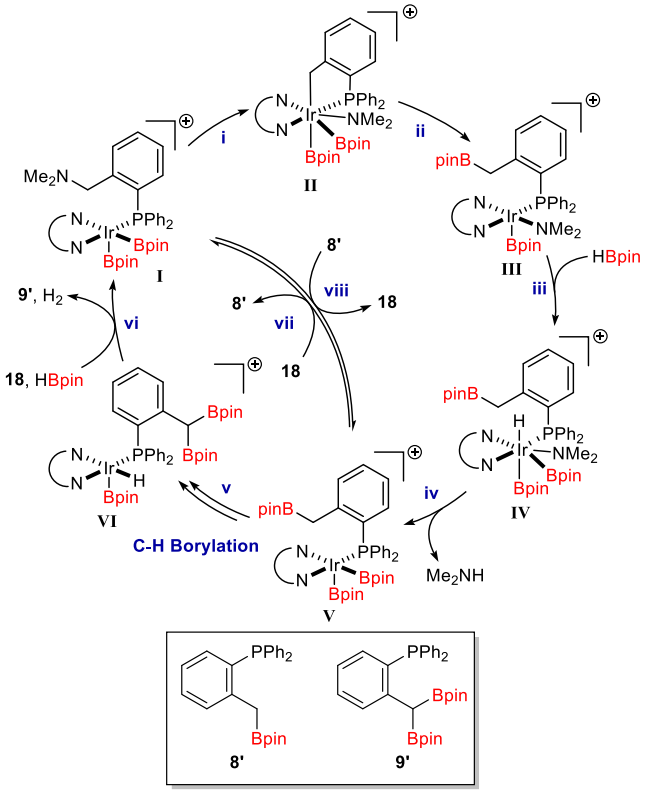


Several C–O and C–N borylation reactions have been reported in the literature. The most prevalent examples include nickel-catalyzed sp^2 and benzylic sp^3 C–N borylations[48-50] of ammonium salts, which provides monoborylated products.[48-50] A related nickel-catalyzed C–O borylation was reported for aryl and benzylic methoxy ethers.[51] In addition, both palladium- and copper-catalyzed borylation of benzylic alcohols have been reported.[52,53] To the best of our knowledge, this is the first example of an iridium-catalyzed C–O or C–N borylation, and the only example that is coupled to a C–H borylation reaction, which uniquely provides bisborylation products.

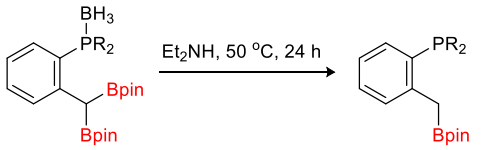
The formation of **9** from **17** and **18** (Scheme 5) is proposed to proceed through initial C–O or C–N borylation, followed by C–H borylation. This conclusion is supported by the identification of 8-10% isolated yields of **8** in the borylation of **17** and **18**, and no apparent formation of the desired α-aminoboronate ester. In this case, the predominant formation of **9** likely results from rapid C–H borylation of **8'** (unprotected **8**) under the reaction conditions. Further support for such a mechanism comes from the reaction of **7** (Scheme 4). Extensive efforts to optimize the selective formation of monoborylation product **8** were unsuccessful, always resulting in more bisborylation product **9** than **8**, even at low conversion of **7** to borylated products. At low conversions, the concentration of **8'** is low, suggesting that the second borylation takes place at a faster rate than dissociation of **8'**. Notably, dicyclohexyl-substituted phosphine **4** can be mono-borylated selectively to form **5** (Scheme 3a). The selective formation of **5** likely results from the increased steric congestion imposed by the cyclohexyl substituents,[54] increasing the relative rate of **5'** dissociating from the catalyst rather than undergoing a second borylation.

Based on these observations, along with the experimental and computational work on C–H borylation reactions,[55-58] a proposed catalytic cycle for the formation of **9** from **18** is provided in Scheme 6. The catalytic cycle starts with phosphine-coordinated iridium(III)bisboryl cation (**I**), which undergoes oxidative addition into the C–N bond to form **II** (step i), which is analogous to previously postulated iridium(V) heptacoordinate complexes. Reductive elimination of **II** forms the C–B bond (step ii), followed by oxidative addition into the H–B bond of pinacolborane (step iii). Reductive elimination of dimethylamine (step iv) provides iridium(III)bisboryl complex **V**, which should have similar properties as **I**. Formation of bisborylated **9'** from **V** then proceeds by C–H activation and C–B bond formation (step v), followed by dissociation of **9'** and regeneration of **I** with pinacolborane (step vi). As stated above, trace formation of **8'** results from slow ligand exchange of **V** (step vii) before C–H activation (step v), returning to the catalytically active **I**.

Scheme 6. Proposed Catalytic Cycle for Borylation of Amine **18**



Scheme 7. Deprotection of Phosphine Boronates **6** and **9**



6 (R = Cy)
9 (R = Ph)

5' (R = Cy), 97%
8' (R = Ph), 91%

In summary, phosphine-directed benzylic C–H borylation has been reported. With a dicyclohexyl-substituted phosphine, conditions have been identified to control for mono- and bisborylation products. In contrast, a diphenyl-substituted phosphine has rapid formation of the bisborylation product. Attempts to obtain secondary C–H borylation of benzylic ethers and amines, proceeded down an unusual pathway, providing C–O and C–N borylation. Deprotection of the phosphine boronates provides unique ambiphilic phosphine boronates, which also result in protodeboration under the reaction conditions. Further investigations into the observed borylation reactivity are underway.

EXPERIMENTAL SECTION

General methods. All procedures involving air- or moisture-sensitive reagents were performed in oven- or flame-dried glassware and under purified nitrogen, either in an inert atmosphere glovebox or by standard Schlenk techniques. In all procedures, unless otherwise noted, concentration was performed by rotary evaporation or by subjecting the material to high vacuum using a Schlenk line. TLC analysis was performed on Whatman 60 Å silica layer fluorescence UV plates. Flash column chromatography was carried out on hand-packed columns of silica gel, 40-63μm, 60 Å.

NMR spectra were collected on a ^{UNITY}Inova spectrometer at 500 MHz or 400 MHz for ^{1}H NMR, 100 or 125 MHz for ^{13}C NMR, 128 MHz for ^{11}B NMR, and 202 MHz for ^{31}P NMR spectroscopy. ^{1}H NMR spectra are referenced to $CDCl_3$ at 7.26 ppm, or to C_6D_6 at 7.16 ppm, or to an internal tetramethylsilane (TMS) standard at 0.00 ppm. The peaks representing the hydgrogens in BH_3 are broad and spread out over a large area, often partially overlapping with other peaks. For this reason, they could not always be identified and were not accounted for in most ^{1}H NMR spectra unless clearly identifiable. The ^{1}H NMR spectral data are reported as follows: chemical shift ppm, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, qn = quintet, hex = hextet, sep = septet, oct = octet, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR spectra are referenced to $CDCl_3$ at 77.0 ppm or to C_6D_6 at 128.0 ppm. Carbon atoms attached to boron are typically not observed and accounted for in the analysis. ^{11}B NMR spectra were referenced to an external $BF_3{\cdot}Et_2O$ sample in $CDCl_3$ or C_6D_6 (0.0 ppm). The ^{11}B NMR spectra were typically processed by adding 15 points of backward linear prediction to remove the glass peaks from the broadband probe and 5 Hz of apodization was applied. ^{31}P NMR spectra were referenced to an external H_3PO_4 sample (0.0 ppm). High Resolution Mass Spectrometry was obtained at the University of California, Irvine Mass Spectrometry Facility.

All solvents were dried and degassed by standard procedures unless employed for extraction or purification. Dioxane was obtained from a solvent purification system, degassed by freeze, pump, thaw cycles (×3), and stored in a glovebox. Tetrahydrofuran was obtained from a solvent purification system, dried over sodium metal and benzophenone, then distilled, followed by freeze, pump, thaw cycles (×3), and stored in a glovebox. Benzene-d_6 was distilled from CaH_2, degassed by freeze, pump, thaw cycles (×3), and stored in a glovebox. Chloroform-*d* was distilled from $CaSO_4$, degassed by freeze, pump, thaw cycles (×3), and stored in a glovebox. Bromo-2(methoxymethyl)benzene, 1.6 M *n*-butyllithium, chlorodiphenylphosphine, 1-bromo-2-ethylbenzene, pinacolborane, bis(1,5-cyclooctadiene)iridium(I) tetrafluoroborate, 3,4,7,8-tetramethyl-1,10-phenanthroline, 1.0 M borane-tetrahydrofuran solution, and phosphines **4**, **7**, **10**, **11**, **12**, and **18** were purchased and employed without purification. The following compounds were synthesized by known methods: (4-fluoro-2-methylphenyl)diphenylphosphane,[61] (5-chloro-2-methylphenyl)diphenylphosphane,[61] (2-ethylphenyl)diphenylphosphine (**16**)[62] and [2-(methoxymethyl)phenyl](diphenyl)phosphine (**17**).[62]

General Procedure A for Benzylic C-H Borylation and Borane Protection of Phosphines:

To a 25 mL PTFE-valved reaction tube with stir bar was added $[Ir(COD)_2]BF_4$ (0.0049 g, 0.006 mmol), 3,4,7,8-tetramethyl-1,10-phenanthroline (0.0024 g, 0.006 mmol), HBpin (0.2100 g, 1.60 mmol), phosphine (0.400 mmol), and dioxane (1.5 mL). After heating in a 130 °C oil bath for 48–72 hours, the reaction flask was transferred into a glovebox and the volatiles were removed *in vacuo*. Dry THF (3.0 mL) was added to the reaction mixture, removed from the glovebox, and cooled to 0 °C under positive nitrogen pressure. A solution of $BH_3{\cdot}THF$ (2.0 mL, 2.0 mmol BH_3, 1.0 M in THF) was added dropwise, then the reaction flask was warmed to room temperature and, after 2 hours, the volatiles were removed *in vacuo.* Purification via silica gel column chromatography provided the corresponding borane-protected phosphine boronate ester.

C–H Borylation and Protection of Dicyclohexyl(2-methylphenyl)phosphine (**5**): General Procedure A was followed with dicyclohexyl(2-methylphenyl)phosphine (0.115 g, 0.400 mmol) for 48 h. Purification by silica gel flash column chromatography (50:50 dichloromethane/hexanes) provided **5** as a white solid (0.104 g, 61%): mp 131.7–135.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 11.9, 8.0, 1H), 7.35 (t, *J* = 6.8, 1H), 7.25 (dd, *J* = 7.6, 2.9, 1H), 7.18 (t, *J* = 7.7, 1H), 2.57 (s, 2H), 2.29 (q, *J* =11.9, 2H), 1.96 (m, 2H), 1.81 (m, 2H), 1.66–1.53 (m, 6H), 1.39–1.10 (m, 10H; s, 12H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.9, 136.0 (d, *J* = 10.7), 131.1 (d, *J* =7.3), 130.6 (d, *J* = 2.4), 124.9 (d, *J* = 10.6), 124.5 (d, *J* = 46.8), 83.7, 34.2 (d, *J* = 32.7), 28.4, 27.3, 27.0 (d, *J* = 5.5), 26.9 (d, *J* = 6.3), 25.8 (d, *J* = 1.5), 24.8; ^{31}P NMR (202 MHz, $CDCl_3$) δ 30.1; ^{11}B{^{1}H} NMR (128 MHz, $CDCl_3$) δ 33.0, –41.9. HRMS (ESI) m/z: $[C_{25}H_{43}B_2O_2P + Na]^+$ Calcd for $C_{25}H_{43}B_2O_2PNa$ 451.3094; Found 451.3087.

Bis C–H Borylation and Protection of Dicyclohexyl(2-methylphenyl)phosphine (**6**): General Procedure A was followed with HBpin (0.580 mL, 4.00 mmol) and dicyclohexyl(2-methylphenyl)phosphine (0.115 g, 0.400 mmol) for 72 h. Purification by silica gel flash column chromatography (50:50 dichloromethane:hexanes) provided **6** as a white solid (0.205 g, 92%): mp 167.2–176.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 13.5, 7.9, 1H), 7.50 (d, *J* = 7.8, 1H), 7.37 (t, *J* = 7.6, 1H), 7.14 (t, *J* = 7.5, 1H), 2.60 (s, 1H), 2.40 (q, *J* = 11.7, 2H), 1.95 (d, *J* = 12.7, 2H), 1.79 (d, *J* = 8.2, 2H), 1.68–1.61 (m, 6H), 1.32–1.15 (m, 10H; s, 12H; s, 12H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.7, 137.1 (d, *J* = 15.8), 131.5 (d, *J* = 6.5), 130.2 (d, *J* = 2.5), 124.2 (d, *J* = 12.2), 123.6 (d, *J* = 48.0), 83.9, 34.0 (d, *J* = 32.5), 29.1, 27.5, 27.0 (d, *J* = 11.4), 26.8 (d, *J* = 11.8), 25.8 (d, *J* = 1.5), 24.9, 24.6; ^{31}P NMR (202 MHz, $CDCl_3$) δ 32.3; ^{11}B{^{1}H} NMR (128 MHz, $CDCl_3$) δ 32.7, –42.9. HRMS (ESI) m/z: $[C_{31}H_{54}B_3O_4P + Na]^+$ Calcd for $C_{31}H_{54}B_3O_4PNa$ 577.3953; Found 577.3954.

C-H Borylation and Protection of Diphenyl(*o*-tolyl)phosphine (**8**): General Procedure A was followed with

HBpin (0.210 g, 1.60 mmol) and diphenyl(*o*-tolyl)phosphine (0.1105 g, 0.400 mmol) for 48 h. Purification by sílica gel flash column chromatography (50:50 dichloromethane:hexanes) provided **8** (0.0182 g, 11%) and **9** (0.0848 g, 39%) as white solids, spectral data for **8**: mp 108.5–115.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (m, 5H), 7.48 (t, *J* = 6.3, 2H), 7.41 (m, 5H), 7.10 (t, *J* = 7.7, 1H), 6.98 (dd, *J* = 11.9, 11.5, 1H), 2.38 (s, 2H), 1.17 (s, 12H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.5 (d, *J* = 10.7), 134.3 (d, *J* = 8.6), 133.2 (d, *J* = 9.4), 131.9 (d, *J* = 8.6), 131.1 (d, *J* = 2.2), 130.9 (d, *J* = 2.2), 129.5 (d, *J* = 57.4), 128.7 (d, *J* = 10.1), 126.7 (d, *J* = 56.7), 125.1 (d, *J* = 9.5), 83.4, 24.7, 21.0 (br s); ^{31}P NMR (202 MHz, $CDCl_3$) δ 21.7; ^{11}B{^{1}H} NMR (128 MHz, $CDCl_3$) δ 32.3, -36.8. HRMS (CI) m/z: $[C_{25}H_{31}B_2O_2P - BH_3]^+$ Calcd for $C_{25}H_{31}B_2O_2P - BH_3$ 402.1925; Found 402.1920.

Bis C-H Borylation and Protection of Diphenyl(*o*-tolyl)phosphine (**9**): General Procedure A was followed with HBpin (0.510 g, 4.00 mmol) and diphenyl(*o*-tolyl)phosphine (0.1105 g, 0.400 mmol for 72 h. Purification by sílica gel flash column chromatography (60:40 dichloromethane:hexanes) provided **8** (0.0124 g, 7%) and **9** (0.1446 g, 67%) as white solids, spectral data for **9**: mp 142.4–149.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.59 (m, 4H), 7.48 (t, *J* = 4.5, 1H), 7.45-7.37 (m, 7H), 7.09-7.01 (m, 2H), 2.66 (s, 1H), 1.14 (s, 12H), 1.13 (s, 12 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 145.6 (d, *J* = 9.4), 133.9 (d, *J* = 10.4), 133.2 (d, *J* = 8.7), 132.71 (d, *J* = 8.2), 130.7 (d, *J* = 2.4), 130.6 (d, *J* = 2.3), 129.6 (d, *J* =57.1), 128.7 (d, *J* = 10.1), 125.5 (d, *J* = 57.3), 124.2 (d, *J* = 10.0), 83.3, 24.6, 22.4 (br s); ^{31}P NMR (202 MHz, $CDCl_3$) δ 19.9 ^{11}B{^{1}H} NMR (128 MHz, $CDCl_3$) δ 32.4, -36.7. HRMS (ESI) m/z: $[C_{31}H_{41}B_3O_4P + Na]^+$ Calcd for $C_{31}H_{41}B_3O_4PNa$ 563.3073; Found 563.3085.

Bis C-H Borylation and Protection of [2-(methoxymethyl)phenyl](diphenyl)phosphine (**9**): General Procedure A was followed with HBpin (0.510 g, 4.00 mmol) and [2-(methoxymethyl)phenyl](diphenyl)phosphine (0.123 g, 0.400 mmol) for 48 h. Purification by sílica gel flash column chromatography (70:30 dichloromethane:hexanes) provided **9** (0.1095 g, 50%) and **8** (0.0165 g, 10%) as white solids; Spectral data matched that reported above for **8** and **9**.

Bis C-H Borylation and Protection of 2-(Diphenylphosphino)-*N,N*-dimethylbenzylamine (**9**): General Procedure A was followed with HBpin (0.510 g, 4.00 mmol) and 2-(Diphenylphosphino)-*N,N*-dimethylbenzylamine (0.115 g, 0.400 mmol) for 72 h. Purification by sílica gel flash column chromatography (60:40 dichloromethane:hexanes) provided **8** (0.0121 g, 8%) and **9** (0.1150 g, 59%) as white solids; Spectral data matched that reported above for **8** and **9**.

Bis C-H Borylation and Protection of (4-fluoro-2-methylphenyl)diphenylphosphine (10): General Procedure A was followed with HBpin (0.512 g, 4.00 mmol), (4-fluoro-2-methylphenyl)diphenylphosphine (0.118 g, 0.400 mmol), $[Ir(COD)_2]BF_4$ (0.0049 g, 0.006 mmol), and 3,4,7,8-tetramethyl-1,10-phenanthroline (0.0024 g, 0.006 mmol) for 72 h. Purification by sílica gel flash column chromatography (50:50 dichloromethane:hexanes) provides **10** as a white solid (0.1243 g, 55%): mp 179.5–186.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.57 (m, 4H), 7.47-7.44 (m, 2H), 7.42-7.38 (m, 4H), 7.23 (dt, J = 11.1, 2.9, 1H), 7.08-7.03 (m, 1H), 6.79-6.76 (m, 1H), 2.68 (s, 1H), 1.13 (s, 24H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 164.3 (d, *J* = 249.4), 148.9 (d, *J* = 10.2), 136.0 (dd, *J* = 11.8, 9.4), 133.1 (d, *J* = 9.5), 130.8, 129.3 (d, *J* = 57.3), 128.8 (d, *J* = 10.1), 121.3 (d, *J* = 59.5), 119.6 (dd, *J* = 21.8, 8.8), 111.7 (dd, *J* = 21.2, 11.7), 83.6, 24.6, 22.5 (br s); ^{31}P NMR (202 MHz, $CDCl_3$) δ 21.0; ^{11}B{^{1}H} NMR (128 MHz, $CDCl_3$) δ 32.1, -36.6. HRMS (ESI) m/z: $[C_{31}H_{41}B_3FO_4P + Na]^+$ Calcd for $C_{31}H_{41}B_3FO_4PNa$ 583.2919; Found 583.2926.

Bis C-H Borylation and Protection of (5-chloro-2-methylphenyl)diphenylphosphine (11): General Procedure A was followed with HBpin (0.512 g, 4.00 mmol), (5-chloro-2-methylphenyl)diphenylphosphine (0.124 g, 0.400 mmol), $[Ir(COD)_2]BF_4$ (0.0049 g, 0.006 mmol), and 3,4,7,8-tetramethyl-1,10-phenanthroline (0.0024 g, 0.006 mmol) for 72 h. Purification by sílica gel flash column chromatography (50:50 dichloromethane:hexanes) provides **11** as a white solid (0.0864 g, 38%): mp 195.3–204.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.58 (m, 4H), 7.49-7.46 (m, 2H), 7.43-7.35 (m, 6H), 6.94 (dd, *J* = 12.0, 2.3, 1H) 2.64 (s, 1H), 1.13 (s, 12H), 1.12 (s, 12H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 144.1 (d, *J* = 9.4), 134.2 (d, *J* = 8.7), 133.2 (d, *J* = 9.5), 133.0 (d, *J* = 10.9), 131.05, 130.7, 130.1 (d, *J* = 12.2), 128.9 (d, *J* = 10.1), 128.8 (d, *J* = 56.2), 128.1 (d, *J* = 55.0), 83.5, 24.6, 24.5; ^{31}P NMR (202 MHz, $CDCl_3$) δ 20.9; ^{11}B{^{1}H} NMR (128 MHz, $CDCl_3$) δ 32.3, -36.9. HRMS (ESI) m/z: $[C_{31}H_{41}B_3ClO_4P + Na]^+$ Calcd for $C_{31}H_{41}B_3ClO_4PNa$ 599.2625; Found 599.2641.

Bis C-H Borylation and Protection of (2-ethylphenyl)diphenylphosphine (16): General Procedure A was followed with HBpin (0.510 g, 4.00 mmol) and (2-ethylphenyl)diphenylphosphine (0.116 g, 0.400 mmol) for 48 h. Purification by sílica gel flash column chromatography (60:40 dichloromethane:hexanes) provides **16** as a white solid (0.0564 g, 25%): mp 162.5–173.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61-7.57 (m, 4 H), 7.52-7.50 (m, 1H), 7.49-7.46 (m, 2H), 7.42-7.39 (m, 5H), 7.25-7.21 (m, 1H), 7.13 (t, *J* = 7.5, 1H), 2.86 (d, *J* = 7.6, 2H), 1.16 (s, 12H), 1.14 (s, 12H), 0.97 (t, *J* = 7.7, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 149.9 (d, *J* = 8.9), 134.8 (d, *J* = 10.7), 133.1 (d, *J* = 9.4), 131.3 (d, *J* = 2.4), 130.8 (d, *J* = 2.4), 129.8 (d, *J* = 57.5), 129.7 (d, *J* = 8.3), 128.6 (d, *J* = 10.1), 126.6 (d, *J* = 54.4), 125.6 (d, *J* = 10.5) 83.0, 30.4 (d, *J* = 6.0), 24.8, 24.5; ^{31}P NMR (202 MHz, $CDCl_3$) δ 21.2; ^{11}B{^{1}H} NMR (128 MHz, $CDCl_3$) δ 29.03, -40.66. HRMS (ESI) m/z: $[C_{32}H_{44}B_3O_4P + Na]^+$ Calcd for $C_{32}H_{44}B_3O_4PNa$ 579.3170; Found 579.3171.

General Procedure B for Deprotection of Phosphine Boronates:

To a flame-dried 10 mL Schlenk flask, equipped with a stir bar and a reflux condenser and backfilled with positive nitrogen pressure, was added the protected phosphine boronate (0.09 mmol) and sparged diethylamine (2.0 mL, 18.0 mmol). After heating to 50 °C in an oil bath for 24 h, the volatiles were removed in vacuo and the flask was pumped into the inert atmosphere glovebox. The reaction mixture was passed through a plug of basic alumina with dichloromethane (5 mL) and concentrated in vacuo to provide the phosphine boronate.

Deprotection of 6 (5'): General Procedure B was followed with **6** (0.050 g, 0.090 mmol) to provide **5'** as a white semi-solid (0.036 g, 97%): ^{1}H NMR (400 MHz, C_6D_6) δ 7.39 (d, *J* = 8.0, 1H), 7.33 (dd, *J* = 7.6, 4.4, 1H), 7.13 (td, J = 7.5, 1.1, 1H), 7.05 (td, J = 7.4, 1.3, 1H), 2.99 (s, 2H), 1.95 (m, 4H), 1.71 (br s, 4H), 1.60 (t, *J* = 14.3, 4H), 1.41-1.12 (m, 10H), 1.10 (s, 12H); ^{13}C{^{1}H} NMR (125 MHz, C_6D_6) δ 147.5 (d, *J* = 28.7), 133.8 (d, *J* = 17.7), 133.0 (d, *J* = 2.7), 130.7 (d, *J* = 5.2), 128.7, 124.8, 83.1, 34.5 (d, *J* = 13.9), 31.0 (d, *J* = 17.4), 29.5 (d, *J* = 8.5), 27.59 (d, *J* = 22.0), 27.57 (d, *J* = 2.0), 26.9, 25.1; ^{31}P NMR (202 MHz, C_6D_6) δ 17.1; ^{11}B{^{1}H} NMR (128 MHz, C_6D_6) δ 33.0. HRMS (ESI) m/z: $[C_{25}H_{28}BO_2P + Na]^+$ Calcd for $C_{25}H_{28}BO_2PNa$ 425.1822; Found 425.1823.

Deprotection of 9 (8'): General Procedure B was followed with **9** (0.050 g, 0.092 mmol) to provide (**8'**) as a white semi-solid (0.034 g, 91%): ^{1}H NMR (400 MHz, C_6D_6) δ 7.42 (m, 4H), 7.25 (m, 1H), 7.13 (ddd, *J* = 7.6, 4.2, 1.2, 1H), 7.06 (m, 7H), 6.89 (td, *J* = 7.5, 1.2, 1H), 2.77 (d, *J* = 2.8, 2H), 1.05 (s, 12H); ^{13}C{^{1}H} NMR (125 MHz, C_6D_6) δ 145.4 (d, *J* = 28.7), 137.7 (d, *J* = 11.2), 136.0 (d, *J* = 10.3), 134.3 (d, *J* = 19.3), 130.5 (d, *J* = 5.3), 129.3, 128.8 (d, *J* = 6.7), 128.7, 125.9, 83.3, 25.0; ^{31}P NMR (202 MHz, C_6D_6) δ 16.5; ^{11}B{^{1}H} NMR (128 MHz, C_6D_6) δ 33.0. HRMS (ESI) m/z: $[C_{25}H_{40}BO_2P + Na]^+$ Calcd for $C_{25}H_{40}BO_2PNa$ 437.2761; Found 437.2758.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Copies of all NMR data for new compounds (PDF)

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REFERENCES

(1) Hartwig, J. F. Borylation and Silylation of C–H Bonds: A Platform for Diverse C–H Bond Functionalizations. *Acc. Chem. Res.* **2012**, *45*, 864.

(2) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. C–H Activation for the Construction of C–B Bonds. *Chem. Rev.* **2010**, *110*, 890.

(3) Xu, L.; Wang, G.; Zhang, S.; Wang, H.; Wang, L.; Liu, L.; Jiao, J.; Li, P. Recent Advances in Catalytic C-H Borylation Reactions. *Tetrahedron* **2017**, *73*, 7123.

(4) Hartwig, J. F. Regioselectivity of the Borylation of Alkanes and Arenes. *Chem. Soc. Rev.* **2011**, *40*, 1992.

(5) Paul, S.; Chotana, G. A.; Holmes, D.; Reichle, R. C.; Maleczka, R. E., Jr.; Smith, M. R., III Ir-Catalyzed Functionalization of 2-Substituted Indoles at the 7-Position: Nitrogen-Directed Aromatic Borylation. *J. Am. Chem. Soc.* **2006**, *128*, 15552.

(6) Boebel, T. A.; Hartwig, J. F. Silyl-Directed, Iridium-Catalyzed *ortho*-Borylation of Arenes. A One-Pot *ortho*-Borylation of Phenols, Arylamines, and Alkylarenes. *J. Am. Chem. Soc.* **2008**, *130*, 7534.

(7) Kawamorita, S.; Ohmiya, H.; Hara, K.; Fukuoka, A.; Sawamura, M. Directed Ortho Borylation of Funtionalized Arenes Catalyzed by a Silica-Supported Compact Phosphine–Iridium System. *J. Am. Chem. Soc.* **2009**, *131*, 5058.

(8) Ishiyama, T.; Isou, H.; Kikuchi, T.; Miyaura, N. *Ortho*-C–H Borylation of Benzoate Esters with Bis(pinacolato)diboron Catalyzed by Iridium–Phoshine Complexes. *Chem. Commun.* **2010**, *46*, 159.

(9) Kawamorita, S.; Ohmiya, H.; Sawamura, M. Ester-Directed Regioselective Borylation of Heteroarenes Catalyzed by a Silica-Supported Iridium Complex. *J. Org. Chem.* **2010**, *75*, 3855.

(10) Ros, A.; Estepa, B.; López-Rodríguez, R.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. Use of Hemilabile N,N Ligands in Nitrogen-Directed Iridium-Catalyzed Borylations of Arenes. *Angew. Chem., Int. Ed.* **2011**, *50*, 11724.

(11) Kawamorita, S.; Miyazaki, T.; Ohmiya, H.; Iwai, T.; Sawamura, M. Rh-Catalyzed *Ortho*-Selective C–H Borylation of *N*-Functionalized Arenes with Silica-Supported Bridgehead Monophosphine Ligands. *J. Am. Chem. Soc.* **2011**, *133*, 19310.

(12) Roering, A. J.; Hale, L. V. A.; Squier, P. A.; Ringgold, M. A.; Wiederspan, E. R.; Clark, T. B. Iridium-Catalyzed, Substrate-Directed C-H Borylation Reactions of Benzylic Amines. *Org. Lett.* **2012**, *14*, 3558.

(13) Ros, A.; López-Rodríguez, R.; Estepa, B.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. Hydrazone as the Directing Group for Ir-Catalyzed Arene Diborylations and Sequential Functionalizations. *J. Am. Chem. Soc.* **2012**, *134*, 4573.

(14) Ghaffari, B.; Preshlock, S. M.; Plattner, D. L.; Staples, R. J.; Maligres, P. E.; Krska, S. W.; Maleczka, R. E., Jr.; Smith, M. R., III Silyl Phosphorus and Nitrogen Donor Chelates for Homogeneous Ortho Borylation Catalysis. *J. Am. Chem. Soc.* **2014**, *136*, 14345.

(15) Crawford, K. M.; Ramseyer, T. R.; Daley, C. J. A.; Clark, T. B. Phosphine-Directed C-H Borylation Reactions: Facile and Selective Access to Ambiphilic Phosphine Boronate Esters. *Angew. Chem., Int. Ed.* **2014**, *53*, 7589.

(16) Ros, A.; Fernández, R.; Lassaletta, J. M. Functional Group Directed C-H Borylation. *Chem. Soc. Rev.* **2014**, *43*, 3229.

(17) Okada, S.; Namikoshi, T.; Watanabe, S.; Murata, M. Ruthenium-Catalyzed *Ortho*-Selective Aromatic C-H Borylation of 2-Arylpyridines with Pinacolborane. *ChemCatChem* **2015**, *7*, 1531.

(18) Saito, Y.; Segawa, Y.; Itami, K. *para*-C-H Borylation of Benzene Derivatives by a Bulky Iridium Catalyst. *J. Am. Chem. Soc.* **2015**, *137*, 5193.

(19) Kuninobu, Y.; Ida, H.; Nishi, M.; Kanai, M. A *meta*-Selective C-H Borylation Directed by a Secondary Interaction between Ligand and Substrate. *Nat. Chem.* **2015**, *7*, 712.

(20) Davis, H. J.; Mihai, M. T.; Phipps, R. J. Ion Pair-Directed Regiocontrol in Transition-Metal Catalysis: A Meta-Selective C-H Borylation of Aromatic Quaternary Ammonium Salts. *J. Am. Chem. Soc.* **2016**, *138*, 12759.

(21) Bisht, R.; Chattopadhyay, B. Formal Ir-Catalyzed Ligand-Enabled Ortho and Meta Borylation of Aromatic Aldehydes via in Situ-Generated Imines. *J. Am. Chem. Soc.* **2016**, *138*, 84.

(22) Li, H. L.; Kuninobu, Y.; Kanai, M. Lewis Acid-Base Interaction-Controlled *ortho*-Selective C-H Borylation of Aryl Sulfides. *Angew. Chem., Int. Ed.* **2017**, *56*, 1495.

(23) Wang, G.; Liu, L.; Wang, H.; Ding, Y.-S.; Zhou, J.; Mao, S.; Li, P. N,B-Bidentate Boryl Ligand-Supported Iridium Catalyst for Efficient Functional-Group-Directed C-H Borylation. *J. Am. Chem. Soc.* **2017**, *139*, 91.

(24) Chattopadhyay, B.; Dannatt, J. E.; Andujar-De Sanctis, I. L.; Gore, K. A.; Maleczka, R. E., Jr.; Singleton, D. A.; Smith, M. R., III Ir-Catalyzed ortho-Borylation of Phenols Directed by Substrate-Ligand Electrostatic Interactions: A Combined Experimental/in Silico Strategy for Optimizing Weak Interactions. *J. Am. Chem. Soc.* **2017**, *139*, 7864.

(25) Su, B.; Zhou, T.-G.; Xu, P.-L.; Shi, Z.-J.; Hartwig, J. F. Enantioselective Borylation of Aromatic C-H Bonds with Chiral Dinitrogen Ligands. *Angew. Chem., Int. Ed.* **2017**, *56*, 7205.

(26) Xu, F.; Duke, O. M.; Rojas, D.; Eichelberger, H. M.; Kim, R. S.; Clark, T. B.; Watson, D. A. Arylphosphonate-Directed Ortho C-H Borylation: Rapid Entry into Highly-Substituted Phosphoarenes. *J. Am. Chem. Soc.* **2020**, *142*, 11988.

(27) Kawamorita, S.; Miyazaki, T.; Iwai, T.; Ohmiya, H.; Sawamura, M. Rh-Catalyzed Borylation of N-Adjacent C(sp^3)-H Bonds with a Silica-Supported Triarylphosphine Ligand. *J. Am. Chem. Soc.* **2012**, *134*, 12924.

(28) Liskey, C. W.; Hartwig, J. F. Iridium-Catalyzed Borylation of Secondary C-H Bonds in Cyclic Ethers. *J. Am. Chem. Soc.* **2012**, *134*, 12422.

(29) Mita, T.; Ikeda, Y.; Michigami, K.; Sato, Y. Iridium-Catalyzed Triple C(sp^3)-H Borylations: Construction of Triborylated sp^3-Carbon Centers. *Chem. Commun.* **2013**, *49*, 5601.

(30) Kawamorita, S.; Murakami, R.; Iwai, T.; Sawamura, M. Synthesis of Primary and Secondary Alkylboronates through Site-Selective C(sp^3)–H Activation with Silica–Supported Monophosphine-Ir Catalysts. *J. Am. Chem. Soc.* **2013**, *135*, 2947.

(31) Li, Q.; Liskey, C. W.; Hartwig, J. F. Regioselective Borylation of the C–H Bonds in Alkylamines and Alkyl Ethers. Observation and Origin of High Reactivity of Primary C–H Bonds Beta to Nitrogen and Oxygen. *J. Am. Chem. Soc.* **2014**, *136*, 8755.

(32) Iwai, T.; Murakami, R.; Harada, T.; Kawamorita, S.; Sawamura, M. Silica-Supported Tripod Triarylphosphane: Application to Transition Metal-Catalyzed C(sp^3)–H Borylations. *Adv. Synth. Catal.* **2014**, *356*, 1563.

(33) Murai, M.; Omura, T.; Kuninobu, Y.; Takai, K. Rhenium-Catalysed Dehydrogenative Borylation of Primary and Secondary C(sp^3)-H Bonds Adjacent to a Nitrogen Atom. *Chem. Commun.* **2015**, *51*, 4583.

(34) Hyland, S. N.; Meck, E. A.; Tortosa, M.; Clark, T. B. α-Amidoboronate Esters by Amide-Directed Alkane C–H Borylation. *Tetrahedron Lett.* **2019**, *60*, 1096.

(35) Yao, W.; Yang, J.; Hao, F. Ru-Catalyzed Selective C(sp^3)-H Monoborylation of Amides and Esters. *ChemSusChem* **2020**, *13*, 121.

(36) Shimada, S.; Batsanov, A. S.; Howard, J. A. K.; Marder, T. B. Formation of Aryl- and Benzylboronate Esters by Rhodium-Catalyzed C–H Bond Functionalization with Pinacolborane. *Angew. Chem., Int. Ed.* **2001**, *40*, 2168.

(37) Ishiyama, T.; Ishida, K.; Takagi, J.; Miyaura, N. Palladium-Catalyzed Benzylic C-H Borylation of Alkylbenzenes with Bis(pinacolato)diboron or Pinacolborane. *Chem. Lett.* **2001**, *30*, 1082.

(38) Mertins, K.; Zapf, A.; Beller, M. Catalytic Borylation of o-Xylene and Heteroarenes via C-H Activation. *J. Mol. Catal. A: Chem.* **2004**, *207*, 21.

(39) Boebel, T. A.; Hartwig, J. F. Iridium-Catalyzed Preparation of Silylboranes by Silane Borylation and Their Use in the Catalytic Borylation of Arenes. *Organometallics* **2008**, *27*, 6013.

(40) Cho, S. H.; Hartwig, J. F. Iridium-Catalyzed Borylation of Secondary Benzylic C–H Bonds Directed by a Hydrosilane. *J. Am. Chem. Soc.* **2013**, *135*, 8157.

(41) Cho, S. H.; Hartwig, J. F. Iridium-Catalyzed Diborylation of Benzylic C-H Bonds Directed by a Hydrosilyl Group: Synthesis of 1,1-Benzyldiboronate Esters. *Chem. Sci.* **2014**, *5*, 694.

(42) Larsen, M. A.; Wilson, C. V.; Hartwig, J. F. Iridium-Catalyzed Borylation of Primary Benzylic C-H Bonds without a Directing Group: Scope, Mechanism, and Origins of Selectivity. *J. Am. Chem. Soc.* **2015**, *137*, 8633.

(43) Palmer, W. N.; Obligacion, J. V.; Pappas, I.; Chirik, P. J. Cobalt-Catalyzed Benyzlic Borylation: Enabling Polyborylation and Functionalization of Remote, Unactivated C(sp^3)-H Bonds. *J. Am. Chem. Soc.* **2016**, *138*, 766.

(44) Jayasundara, C. R. K.; Sabasovs, D.; Staples, R. J.; Oppenheimer, J.; Smith, M. R., III; Maleczka, R. E., Jr. Cobalt-Catalayzed C-H Borylation of Alkyl Arenes and Heteroarenes Including the First Selective Borylations of Secondary Benzylic C-H Bonds. *Organometallics* **2018**, *37*, 1567.

(45) Wright, S. E.; Richardson-Solorzano, S.; Stewart, T. N.; Miller, C. D.; Morris, K. C.; Daley, C. J. A.; Clark, T. B. Accessing Ambiphilic Phosphine Boronates through C-H Borylation by an Unforseen Cationic Iridium Complex. *Angew. Chem., Int. Ed.* **2019**, *58*, 2834.

(46) Wen, J.; Wang, D.; Qian, J.; Wang, D.; Zhu, C.; Zhao, Y.; Shi, Z. Rhodium-Catalyzed P^{III}-Directed *ortho*-C–H Borylation of Arylphosphines. *Angew. Chem., Int. Ed.* **2019**, *58*, 2078.

(47) Fukuda, K.; Iwasawa, N.; Takaya, J. Ruthenium-Catalyzed ortho C–H Borylation of Arylphosphines. *Angew. Chem., Int. Ed.* **2019**, *58*, 2850.

(48) Hu, J.; Sun, H.; Cai, W.; Pu, X.; Zhang, Y.; Shi, Z. Nickel-Catalyzed Borylation of Aryl- and Benzyltrimethylammonium Salts via C-N Bond Cleavage. *J. Org. Chem.* **2016**, *81*, 14.

(49) Zhang, H.; Hagihara, S.; Itami, K. Making Dimethylamino a Transformable Directing Group by Nickel-Catalyzed C-N Borylation. *Chem. Eur. J.* **2015**, *21*, 16796.

(50) Basch, C. H.; Cobb, K. M.; Watson, M. P. Nickel-Catalyzed Borylation of Benzylic Ammonium Salts: Stereospecific Synthesis of Enantioenriched Benzylic Boronates. *Org. Lett.* **2016**, *18*, 136.

(51) Zarate, C.; Manzano, R.; Martin, R. *Ipso*-Borylation of Aryl Ethers via Ni-Catalyzed C-OMe Cleavage. *J. Am. Chem. Soc.* **2015**, *137*, 6754.

(52) Cao, Z.-C.; Luo, F.-X.; Shi, W.-J.; Shi, Z.-J. Direct Borylation of Benzyl Alcohol and its Analogues in the Absence of Bases. *Org. Chem. Frontiers* **2015**, *2*, 1505.

(53) Mao, L.; Szabó, K. J.; Marder, T. B. Synthesis of Benzyl-, Allyl-, and Allenyl-boronates via Copper-Catalyzed Borylation of Alcohols. *Org. Lett.* **2017**, *19*, 1204.

(54) Tolman, C. A. Phosphorus Ligand Exchange Equilibria on Zerovalent Nickel. A Dominant Role for Steric Effects. *J. Am. Chem. Soc.* **1970**, *92*, 2956.

(55) Tamura, H.; Yamazaki, H.; Sato, H.; Sakaki, S. Iridium-Catalyzed Borylation of Benzene with Diboron. Theoretical Elucidation of Catalytic Cycle Including Unusual Iridium(V) Intermediate. *J. Am. Chem. Soc.* **2003**, *125*, 16114.

(56) Boller, T. M.; Murphy, J. M.; Hapke, M.; Ishiyama, T.; Miyaura, N.; Hartwig, J. F. Mechanism of the Mild Functionalization of Arenes by Diboron Reagents Catalyzed by Iridium Complexes. Intermediacy and Chemistry of Bipyridine-Ligated Iridium Trisboryl Complexes. *J. Am. Chem. Soc.* **2005**, *127*, 14263.

(57) Ghaffari, B.; Vanchura, B. A., II; Chotana, G. A.; Staples, R. J.; Holmes, D.; Maleczka, R. E., Jr.; Smith, M. R., III Reversible Borylene Formation from Ring Opening of Pinacolborane and Other Intermediates Generated from Five-Coordinate Tris-Boryl Complexes: Implications for Catalytic C-H Borylation. *Organometallics* **2015**, *34*, 4732.

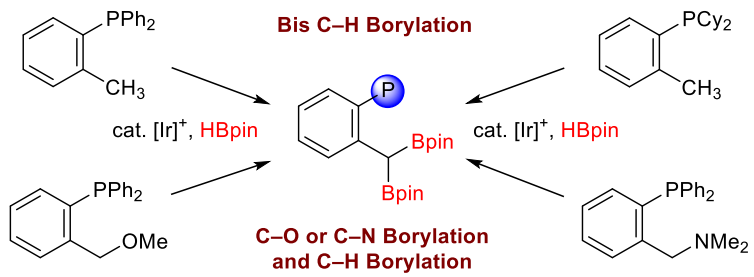
(58) Green, A. G.; Liu, P.; Merlic, C. A.; Houk, K. N. Distortion/Interaction Analysis Reveals the Origins of Selectivities in Iridium-Catalyzed C-H Borylation of Substituted Arenes and 5-Membered Heterocycles. *J. Am. Chem. Soc.* **2014**, *136*, 4575.

(59) Fontaine, F.-G.; Rochette, E. Ambiphilic Molecules: From Organometallic Curiosity to Metal-Free Catalysts. *Acc. Chem. Res.* **2018**, *51*, 454.

(60) Bouhadir, G.; Bourissou, D. Complexes of Ambiphilic Ligands: Reactivity and Catalytic Applications. *Chem. Soc. Rev.* **2016**, *45*, 1065.

(61) Wen, J.; Dong, B.; Zhu, J.; Zhao, Y.; Shi, Z. Revealing Silylation of C(sp^2)/C(sp^3)–H Bonds in Arylphosphines by Ruthenium Catalysis. *Angew. Chem., Int. Ed.* **2020**, *59*, 10909.

(62) Singer, R. A.; Tom, N. J.; Frost, H. N.; Simon, W. M. Discovery and Synthesis of Novel Phosphine-Based Ligands for Aryl Aminations. *Tetrahedron Lett.* **2004**, *45*, 4715.


PPh2
CH3
Bis C–H Borylation
PCy2
CH3
cat. [Ir]+, HBpin
P
Bpin
Bpin
cat. [Ir]+, HBpin
PPh2
OMe
C–O or C–N Borylation
and C–H Borylation
PPh2
NMe2