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Insights into Activation of Cobalt Pre-Catalysts for C(*sp*²)–H Functionalization

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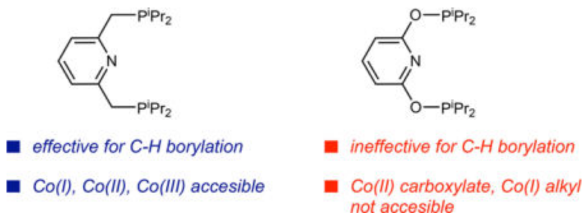
Abstract

The activation of readily prepared, air-stable cobalt (II) bis(carboxylate) pre-catalysts for the functionalization of C(sp^2)–H bonds has been systematically studied. With the pyridine bis(phosphine) chelate, ^{iPr}PNP, treatment of **1-($O_2C^tBu)_2$** with either B_2Pin_2 or HBPin generated cobalt boryl products. With the former, reduction to (^{iPr}PNP)Co^IBPin was observed while with the latter, oxidation to the cobalt(III) dihydride boryl, *trans*-(^{iPr}PNP)$Co(H)_2$BPin occurred. The catalytically inactive cobalt complex, $Co[PinB(O_2C^tBu)_2]2$, accompanied formation of the cobalt-boryl products in both cases. These results demonstrate that the pre-catalyst activation from cobalt(II) bis(carboxylates), although effective and utilizes an air-stable precursor, is less efficient than activation of cobalt(I) alkyl or cobalt(III) dihydride boryl complexes, which are quantitatively converted to the catalytically relevant cobalt(I) boryl. Related cobalt(III) dihydride silyl and cobalt(I) silyl complexes were also synthesized from treatment of *trans*-(^{iPr}PNP)$Co(H)_2$BPin and (^{iPr}PNP)CoPh with $HSi(OEt)_3$, respectively. No catalytic silylation of arenes was observed with either complex likely due to the kinetic preference for reversible C–H reductive elimination rather than product- forming C–Si bond formation from cobalt(III). Syntheses of the cobalt(II) bis(carboxylate) and cobalt(I) alkyl of ^{iPr}PONOP, a pincer where the methylene spacers have been replaced by oxygen atoms, were unsuccessful due to deleterious P–O bond cleavage of the pincer. Despite their structural similarity, the rich catalytic chemistry of ^{iPr}PNP was not translated to ^{iPr}PONOP due to the inability to access stable cobalt precursors as a result of ligand decomposition via P–O bond cleavage.

Graphical abstract



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Dedicated to Professor Robert Bergman with congratulations on the Wolf Prize.

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Keywords

C–H activation; borylation; cobalt; PNP ligand; PONOP ligand

1. Introduction

The selective functionalization of carbon-hydrogen bonds with soluble transition metal complexes is of long-standing interest in organic chemistry and catalysis.[1] Among the many methods now developed, metal-catalyzed borylation of arene C(sp^2)–H bonds is among the most powerful owing to orthogonal selectivity to traditional electrophilic aromatic substitution and the synthetic versatility of the resulting arylboronate products.[2,3] Precious metal catalysts, particularly those based on iridium, are the most commonly used.[2] Increased emphasis on sustainable catalytic methods has generated considerable interest in developing C–H borylation catalysts with earth abundant transition metals such as iron[4] and cobalt.[5] Our laboratory has evaluated a variety of cobalt complexes bearing tridentate ligands[5] and discovered that electron-rich bis(phosphino)pyridine (^{iPr}PNP) chelates[6] are the most effective (Scheme 1).[5a,7]

Detailed mechanistic studies on the [(^{iPr}PNP)Co] family of compounds support a pathway involving the borylated cobalt (I) boryl, 4-BPin-(^{iPr}PNP)CoBPin, as responsible for activation of the C(sp^2)–H bond of substituted pyridines and arenes with B_2Pin_2 (Pin=pinacolate) as the boron source. Modification of the 4-position of the pincer preceded borylation of the substrate.[8] A cobalt(I)-boryl compound was also identified as the C(sp^2)–H activating species during the borylation of 5-membered heteroarenes with HBPin but competing borylation of the cobalt pincer complex was not observed.[9] With these heteroarenes and boron source, the catalyst resting state is the cobalt(III) complex, *trans*-(^{iPr}PNP)Co(H)$_2$BPin.

An important but often overlooked feature of these compounds is that C–H borylation catalysis can be initiated by (^{iPr}PNP)cobalt complexes in different oxidation states. Cobalt(I) alkyl,[5a] cobalt(III) dihydride boryl,[7,8] as well as cobalt(II) bis(carboxylates)[7,10] have all been identified as effective pre-catalysts for this transformation (Scheme 1). Successful catalysis initiated from cobalt precursors across three oxidation states highlights the electronic versatility of first row metals that can be leveraged for distinct reactivity. The air-stability of (^{iPr}PNP)Co(O_2CR)$_2$ compounds and their ease of synthesis from commercially available Co(O_2CR)$_2$ and the free chelate, without the need for pyrophoric alkyl lithium or highly reactive and reducing main group hydride reagents, makes them attractive for applications in synthesis.

The activation mode of [(^{iPr}PNP)Co(I)] alkyl pre-catalysts is well understood as stoichiometric experiments have established quantitative formation of (^{iPr}PNP)CoBPin (**1-BPin**) upon treatment with either HBPin or B_2Pin_2. A sequence involving oxidative addition of a B–H or B–B followed by H–H or H–B reductive elimination, possibly involving phosphine dissociation,[11] generates the intermediate responsible for activation of the C(sp^2)–H bond of the substrate (Schemes 2a and 2b).[5a,8,9]

Despite a mature understanding of how (^{iPr}PNP)cobalt(I) alkyl and cobalt(III) dihydride boryl pre-catalysts enter the C(sp^2)–H borylation cycle, little is known about how the related cobalt(II) bis(carboxylates) undergo activation with HBPin and B_2Pin_2 (Scheme 2c). It is also non-obvious if the same cobalt(I) active species form and if so, how the reduction from Co(II) to Co(I) occurs.[12] Here we describe systematic studies to understand the activation of (^{iPr}PNP)Co($O_2C^tBu)_2$ with both B_2Pin_2 and HBPin. Attempted synthesis of a related cobalt(II) bis(carboxylate) where the methylene subunits of the pincer were replaced with oxygen atoms, (^{iPr}PONOP)Co($O_2C^tBu)_2$, were unsuccessful and resulted in P–O bond cleavage of the ligand and extrusion of the carboxylate groups on the cobalt to yield a new four-coordinate modified ligand complex.

2. Results and Discussion

2.1. Reaction of 1-($O_2C^tBu)_2$ with B_2Pin_2 and HBPin

Stoichiometric studies were conducted with the 4-methyl substituted variant of the cobalt(II) pre-catalyst, (4-Me-^{iPr}PNP) Co($O_2C^tBu)_2$ **(1-$O_2C^tBu)_2$**,[5] because of its established *ortho* to fluorine selectivity in the C(sp^2)–H borylation of fluoroarenes and its resistance to deactivation through catalyst borylation.[8] Addition of ten equiv. of B_2Pin_2 to a THF-[d_8] solution of **(1-$O_2C^tBu)_2$** at 23°C produced no reaction as judged by ^{1}H NMR spectroscopy. Heating the mixture to 80°C for 1 hour resulted in formation of the cobalt(I) boryl dinitrogen complex, (4-Me-^{iPr}PNP)CoBPin(N_2)$_2$ **1-BPin(N_2)**,[8] Scheme 3a). It is possible that reduction of Co(II) to Co(I) occurs by initial formation of an unobserved cobalt(II) diboryl,[13] which undergoes B–B reductive elimination to Co(0) and subsequent comproportionation to two equivalents of Co(I). If operative, this mode of pre-catalyst activation is analogous to the B_2Pin_2 mediated reduction of $(Cy_3P)_2Pd(OAc)_2$ to $(Cy_3P)_2Pd$,[14a] although comproportionation was not observed.[14b] Likewise, treatment of a THF-[d_8] solution of **1-($O_2C^tBu)_2$** with four equiv. of HBPin at 23°C produced 1-(H)$_2$BPin in 68% yield. A paramagnetic cobalt byproduct, assigned as Co[PinB($O_2C^tBu)_2]_2$, was also observed in 32% yield. This product is analogous to Co[PinB(OAc)$_2$]$_2$,[5d] a byproduct identified following treatment of terpyridine cobalt(II) bis(acetate) complexes with HBPin. These observations demonstrate that both B_2Pin_2 and HBPin are sufficient activators and formal reductants for generating cobalt(I) boryl complexes from cobalt(II) precursors.

2.2. Reactions of 1-(H)$_2$BPin and 1-Ph with HSi(OEt)$_3$

The reactivity of **1-($O_2C^tBu)_2$** with silanes was also explored to evaluate the potential of [4-Me-(^{iPr}PNP)Co] compounds for catalytic C(sp^2)–H silylation chemistry.[15] Treatment of **1-($O_2C^tBu)_2$** with two equivalents of HSi(OEt)$_3$ at 23°C in benzene-[d_6] for 48 hours produced an intractable mixture of compounds. An alternative route to a cobalt silyl compound was explored by reversible reductive elimination-oxidative addition from a well-defined cobalt(III) compound. Addition of 1 equivalent of HSi(OEt)$_3$ to a benzene-[d_6] solution of **1-(H)$_2$BPin** produced a new diamagnetic product identified as the cobalt(III) compound, **1-(H)$_2$Si(OEt)$_3$** (Scheme 4a).[16] A diagnostic triplet centered at −9.02 ppm was observed in the benzene-[d_6] 1H NMR spectrum corresponding to the Co–H. A single, sharp ^{31}P resonance was observed at 98.67 ppm, consistent with formation of a six-coordinate [(^{iPr}PNP)Co(III)] compound.[5a,8,17]

The synthesis of cobalt-silyl compounds was also explored from other [(^{iPr}PNP)Co(I)] sources. Addition of one equivalent of $HSi(OEt)_3$ to a benzene-[d_6] solution of 4-Me(^{iPr}PNP) $CoCH_3$, **1-CH_3**[8] at 23°C and monitoring the progress of the reaction for 16 hours by ^1H and ^{31}P NMR spectroscopies established formation of a new, diamagnetic cobalt compound, tentatively assigned as the cobalt(I) silyl[18] dinitrogen compound, **1-$Si(OEt)_3(N_2)$**. Other unidentified cobalt compounds accompanied formation of **1-$Si(OEt)_3(N_2)$**. The cobalt silyl compound exhibits a ^{31}P NMR resonance at 76.39 ppm, a value typical for Co(I) complexes of this type,[5a,8,17] and a ν_{N2} at 2054 cm^{-1} in benzene-d_6 solution, diagnostic of dinitrogen coordination.[8] **1-$Si(OEt)_3(N_2)$** was also generated more cleanly from addition of $HSi(OEt)_3$ to 4-Me(^{iPr}PNP)CoPh (**1-Ph**) at 23°C for 15 minutes (Scheme 4b). Evaluation of **1-$(O_2C^tBu)_2$, 1-$(H)_2$BPin** and **1-CH_3** for the catalytic C–H silylation of benzofuran with $HSi(OEt)_3$ at 80°C both in the presence and in the absence of cyclohexene as an acceptor[15] (see SI for details) resulted in no evidence for formation of silylated products with complete recovery of the arene. The observed lack of reactivity may be a result of the kinetic preference of the cobalt(III) intermediate to preferentially undergo reversible C–H reductive elimination rather than product-forming C–Si bond formation. Such a pathway is supported by the synthesis of **1-$Si(OEt)_3(N_2)$** from **1-Ph** where (^{iPr}PNP)Co(Ph)$Si(OEt)_3$H is likely an intermediate that generates (^{iPr}PNP)Co$Si(OEt)_3$ exclusively.

2.3. Chemistry of (^{iPr}PONOP) Cobalt Compounds

The synthesis of cobalt(II) bis(carboxylate) compounds of ^{iPr}PONOP,[19] where the [CH_2] linkers have been replaced with oxygen atoms, was also explored. This ligand was of interest due to its relative ease of synthesis and potentially distinct electronic properties and coordination preferences as compared to ^{iPr}PNP. Previous work from Schrodi[20a] and coworkers have demonstrated that iPrPONOP-supported iron carbonyl complexes contain a more electron deficient metal center relative to the ^{iPr}PNP-variant.[20b] If similar properties translated on to cobalt, isolable Co(I) complexes would be expected.

Addition of ^{iPr}PONOP to anhydrous cobalt pivalate[21] did not yield the anticipated cobalt(II) bis(carboxylate), (^{iPr}PONOP)Co$(O_2C^tBu)_2$. Instead, the planar cobalt compound **2** was isolated in 36% yield as orange crystals arising from P–O bond cleavage of the pincer upon metalation (Scheme 5). The fate of the remainder of one ^{iPr}PONOP ligands has not been determined. Notably, metalation of ^{iPr}PONOP with $CoCl_2$ has been reported to yield (^{iPr}PONOP)$CoCl_2$, 2-Cl_2,[22] suggesting that the metal carboxylates play a role in the ligand degradation process. Magnetic susceptibility measurements on 2 are consistent with an S=1/2 ground state (μ_{eff}=1.8 μ_B, 23°C). Cooling a saturated ether solution of 2 at −35 C produced crystals suitable for X-ray diffraction and a solid-state representation of 2 is shown in Figure 1.

Complex **2** was evaluated for the C(sp^2)–H borylation of a selection of heteroarenes using HBPin as the boron source. Stirring a mixture of neat benzofuran, HBPin and 5 mol% of **2** at 80°C for 16 hours resulted in complete conversion to the 2-benzofuranyl product (Scheme 6). No catalytic turnover was observed with other five-membered heteroarenes including: substituted furans, benzothiophene, 2-methylthiophene and *N*-methylindole.

Because the synthesis of the targeted cobalt bis(carboxylate) complex of ^{iPr}PONOP was not synthesized through standard methods, preparation of a well-defined cobalt(I) alkyl containing this pincer was explored. Addition of two equivalents of $LiCH_2SiMe_3$ to a toluene solution of (^{iPr}PONOP) $CoCl_2$,[22] **2-Cl₂**, produced an intractable mixture of products arising from P–O bond cleavage within the chelate as evidenced by formation of $iPr_2PCH_2SiMe_3$ (Scheme 7a). The synthesis and alkylation (^{iPr}PONOP)CoCl was also pursued, owing to the rich chemistry associated with related (^{iPr}PNP) CoR (R=H, alkyl, aryl) compounds.[23] Unfortunately, addition of one equivalent of $LiCH_2SiMe_3$ to a toluene solution of (^{iPr}PONOP)CoCl, **2-Cl**, also produced an intractable mixture of cobalt products. Similarly, $iPr_2PCH_2SiMe_3$ was identified by ^{1}H and ^{31}P NMR spectroscopy, consistent with P–O bond cleavage in the chelate (Scheme 7b).[24]

3. Conclusions

Studies on the activation of the readily prepared, air-stable C(*sp*^{2})–H arene borylation pre-catalyst, **1-($O_2C^tBu)_2$**, with both B_2Pin_2 and HBPin were conducted. With B_2Pin_2, reduction to the cobalt(I) boryl, **1-BPin**, was observed while with HBPin oxidation to the cobalt(III) dihydride boryl, **1-H_2 (BPin)** occurred. In both cases, formation of the catalytically inactive $Co[PinB(O_2C^tBu)_2]_2$ accompanied generation of the cobalt boryl compounds. Related pincer-ligated cobalt(I) and cobalt(III) silyl complexes have been synthesized from treatment of **1-Ph** and **1-$(H)_2$BPin** with $HSi(OEt)_3$, respectively. Despite their structural resemblance to the cobalt boryl compounds, no C–H functionalization reactivity was observed. Attempted synthesis of the cobalt(II) bis(carboxylate) with the related pincer, ^{iPr}PONOP, resulted in the isolation of complex **2** arising from extrusion of carboxylate ligands on cobalt and P–O bond cleavage of the chelate. Despite the structural similary of ^{iPr}PNP and ^{iPr}PONOP, the rich catalytic chemistry of ^{iPr}PNP cobalt compounds was not observed with ^{iPr}PONOP due to the deleterious P–O bond cleavage of the chelate. As a result, stable cobalt pre-catalysts with this pincer have not yet been synthesized.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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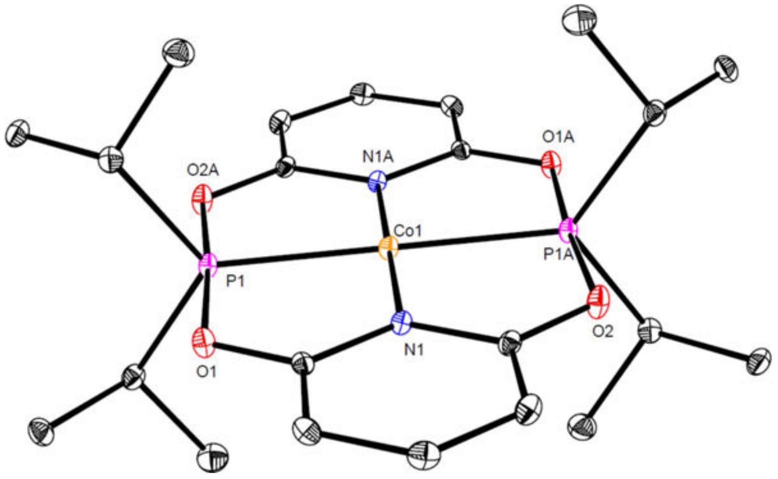
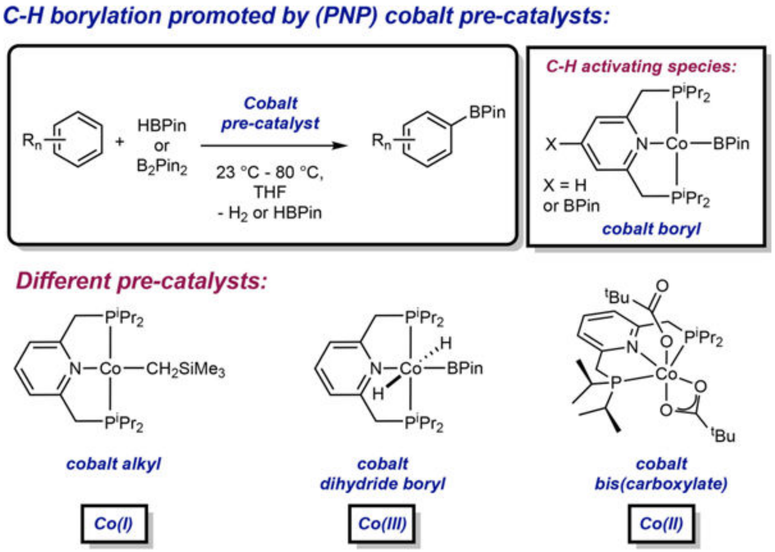


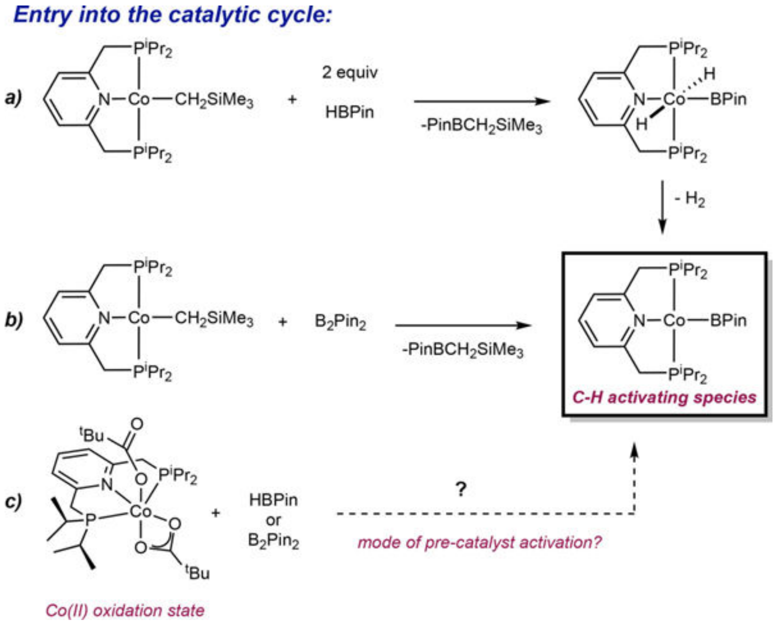
Figure 1.

Solid state structure of **2** at 30% probability ellipsoids. Hydrogen atoms were omitted for clarity.



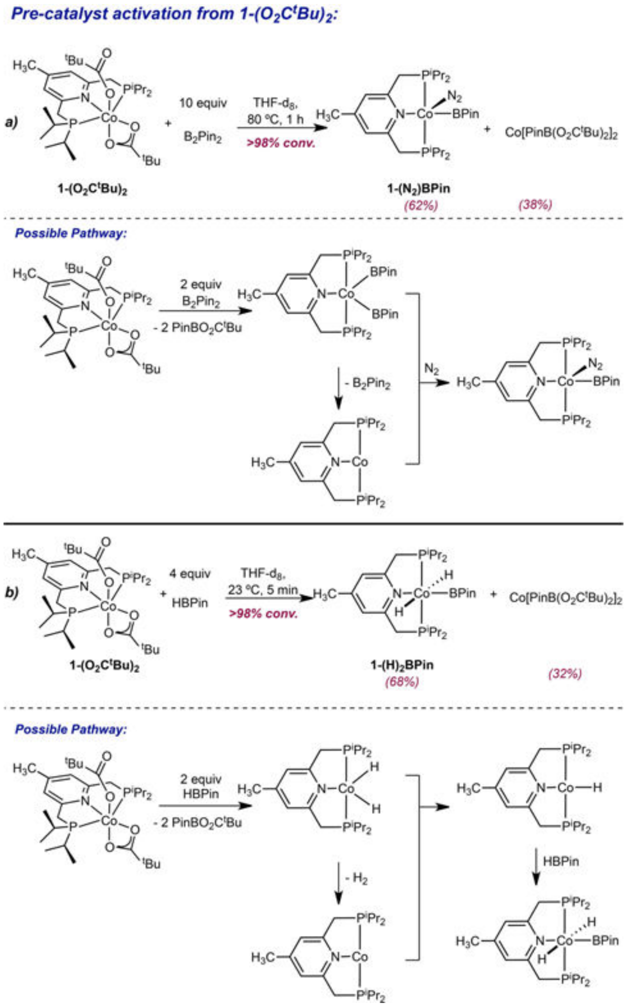
Scheme 1.

(PNP)cobalt pre-catalysts employed for C–H borylation of arenes. The parent pincer ligand (X=H) is shown for the different catalysts for simplicity.



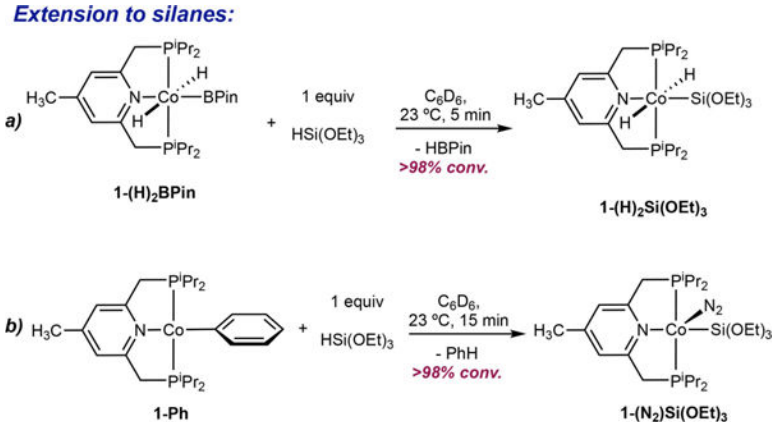
Scheme 2.

Different activation modes of pincer cobalt borylation catalysts.



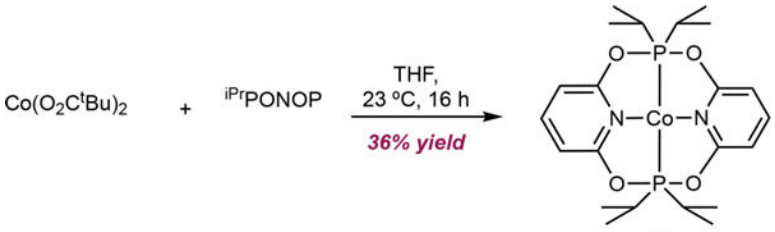
Scheme 3.

Stoichiometric reactions of **1-($O_2C^tBu)_2$** with B_2Pin_2 and HBPin.



Scheme 4.

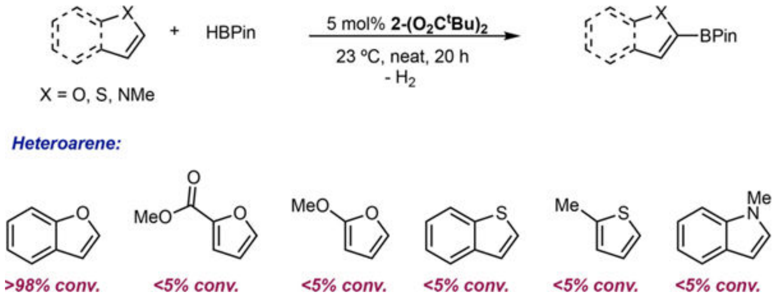
Stoichiometric reactions of **1-(H)$_2$BPin** and **1-Ph** with HSi (OEt)$_3$.



2

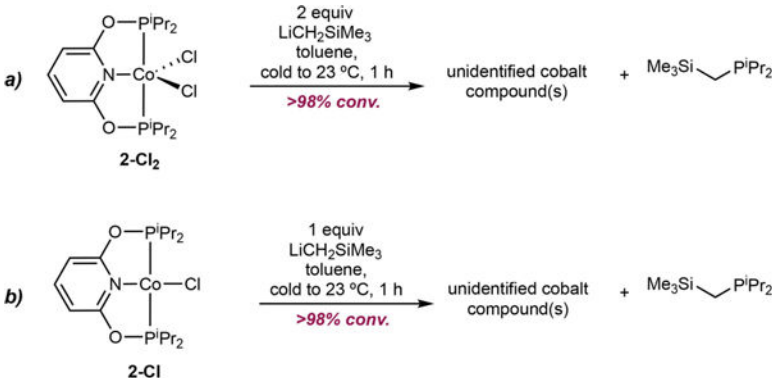
Scheme 5.

Synthesis of **2**.



Scheme 6.

Evaluation of **2** for catalytic C–H borylation.



Scheme 7.

Attempted synthesis of a cobalt alkyl derived from ^{iPr}PONOP.