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Alkene Isomerization–Hydroboration Promoted by Phosphine-Ligated Cobalt Catalysts

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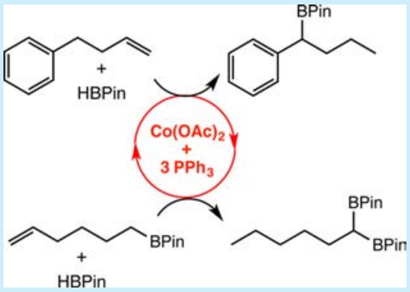
Supporting Information

ABSTRACT: Generated in situ from air-stable cobalt precursors or readily synthesized using $NaHBEt_3$, $(PPh_3)_3CoH(N_2)$ was found to be an effective catalyst for the hydroboration of alkenes. Unlike previous base-metal catalysts for alkene isomerization–hydroboration which favor the incorporation of boron at terminal positions, $(PPh_3)_3CoH(N_2)$ promotes boron incorporation adjacent to π-systems even in substrates where the alkene is at a remote position, enabling a unique route to 1,1-diboron compounds from α,ω-dienes.

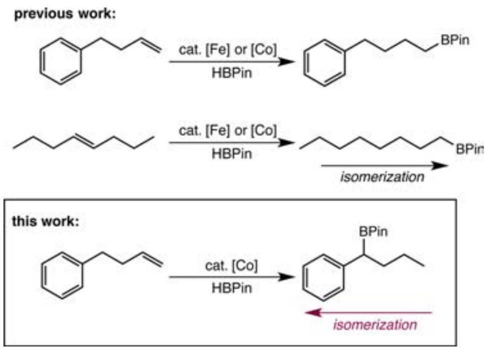


Boron-containing molecules are valuable synthons for a range of organic transformations.[1] Organoboron compounds are the nucleophilic component of Suzuki–Miyaura cross couplings, one of the most widely employed methods for carbon–carbon bond formation in the pharmaceutical industry.[2] While aryl boronates are the most commonly used substrates,[3] recent advances in cross-coupling catalysis have extended the method to alkyl and benzylic organoboronates often operating with high enantiospecificity.[4]

The advent and maturation of these methods motivates efficient, selective, and sustainable synthetic routes to alkyl boronate esters. The metal-catalyzed hydroboration of alkenes is an attractive approach for the synthesis of secondary alkyl boronate esters given its vast precedent and atom economy.[1] Organometallic and coordination complexes of rhodium, iridium, and group 4 metallocenes have dominated the catalyst landscape but suffer from potential economic and environmental drawbacks and, in many cases, have limited substrate scope or offer poor selectivity.[1] Renewed interest in base-metal catalysis has resulted in the discovery of copper,[5] iron, and cobalt catalysts for alkene hydroboration.[6−10] The iron and cobalt catalysts offer the distinguishing feature of promoting alkene isomerization–hydroboration with high terminal selectivity. In many cases, no matter the starting position of the C═C bond, carbon–boron bond formation is highly selective for the terminal position of the alkyl chain (Scheme 1).

The majority of these catalysts are supported by redox-active or strongly π-acidic ligands,[10] raising the question if whether more classical innocent-type ligands are also effective. Understanding such influences will open the scope of metal–ligand combinations available for base-metal-catalyzed hydroboration and ultimately may enable the discovery of new catalysts. Here, we describe the catalytic performance of cobalt–phosphine complexes in alkene hydroboration and highlight features distinct from those with redox-active supporting ligands.

Scheme 1. Iron- and Cobalt-Catalyzed Alkene Isomerization–Hydroboration



Our studies commenced with the evaluation of combinations of commercially available and ideally air-stable cobalt precursors and phosphine ligands to promote catalytic carbon–boron bond formation. Inspired by our recent observation of cobalt-catalyzed reduction of formate using silanes,[11] cobalt(II) bis(carboxylates) were selected as the base-metal precursors. Reagents of this type are air-stable and among the most inexpensive sources of cobalt. Phosphines were chosen as supporting ligands because of their commercial availability, their electronic and steric modularity, and the recent observation that cobalt complexes supported by strong field ligands promote catalytic C–H borylation.[12,13] Benzofuran was selected as the initial substrate for evaluation as both alkene hydroboration and C–H borylation reactions are possible.

A THF solution of benzofuran and 1.6 equiv of HBPin (Pin = pinacolate) was stirred under an N_2 atmosphere with 5 mol % of cobalt(II) acetate and 15 mol % of PPh_3 for 72 h at 23 °C.

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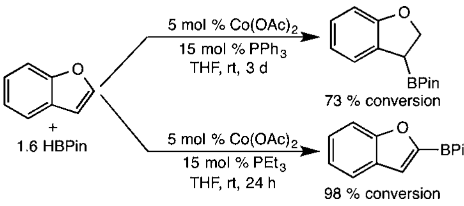
Analysis of the isolated product by multinuclear NMR spectroscopy established formation of 2,3-dihydrobenzofuran-3-ylpinacolborane, arising from selective hydroboration of the alkene with carbon−boron bond formation at the benzylic position (Scheme 2, top). To our knowledge, the selective hydroboration of this substrate has not been reported. Performing the analogous reaction with $(^{Mes}PDI)CoCH_3$, an active alkene hydroboration catalyst[12] yielded trace amounts of C−H borylation products rather than alkene hydrometalation.

Scheme 2. Selective Catalytic Hydroboration or Borylation of Benzofuran with HBPin Promoted by $Co(OAc)_2$/Phosphine Mixtures



The identity of the added phosphine had a dramatic effect on the reaction outcome. Replacing PPh_3 with PEt_3 resulted in quantitative and selective C−H borylation, demonstrating that more electron-rich phosphines promote carbon−hydrogen functionalization rather than hydrofunctionalization of the alkene. The results highlight the versatility of the procedure as the chemoselectivity of the reaction can be completely altered by choice of added ligand.

The observation of a unique cobalt-catalyzed hydroboration of benzofuran prompted investigation into the nature of the active base-metal catalyst responsible for carbon−boron bond formation. Monitoring the hydroboration of benzofuran with $Co(OAc)_2$ and PPh_3 by ^{31}P NMR spectroscopy indicated that the bulk of the phosphine present (>90%) was free PPh_3. An unidentified paramagnetic cobalt compound, likely containing only [OBPin] and carboxylate ligands, exhibited ^1H NMR resonances at 15.16 and −25.64 ppm. A relatively minor peak at −21.20 ppm in the ^1H NMR spectrum and corresponding ^{31}P NMR resonance at 48.0 ppm were assigned to $(PPh_3)_3CoH(N_2)$, a compound originally reported by Sacco and Rossi.[14−17] It is likely that $(PPh_3)_3CoH(N_2)$ arises from activation and reduction of the cobalt acetate groups by HBPin driven by formation of strong B−O bonds. A similar strategy has been employed for the activation of palladium acetate precatalysts for cross-coupling reactions[18] and more recently with $Ni(OAc)_2$ for generating C−H borylation catalysts.[19]

Previous studies with $(PPh_3)_3CoH(N_2)$ have demonstrated catalytic hydrosilylation of 1-hexene with $SiH(OEt)_3$,[20] and related alkene hydroboration reactions therefore seemed plausible. To test this hypothesis, a new, reliable synthetic route to $(PPh_3)_3CoH(N_2)$ was devised whereby $(PPh_3)_2CoCl_2$ was treated with 2 equiv of $NaHBEt_3$ in the presence of PPh_3 (Scheme 3). This new method is highly reproducible and eliminates the need for difficult to handle and ill-defined aluminum reductants used in the original route.[14,21] During the course of these investigations, higher resolution X-ray crystallographic data were collected on the compound and are reported in the Supporting Information.

The catalytic alkene hydroboration activity of $(PPh_3)_3CoH(N_2)$ was then evaluated using HBPin and benzofuran as substrates (Table 1, entry 1). Dramatically improved activity over the in situ method was observed as complete conversion, and an 84% isolated yield was obtained after 2 h at 23 °C.

Scheme 3. Synthesis of $(PPh_3)_3CoH(N_2)$

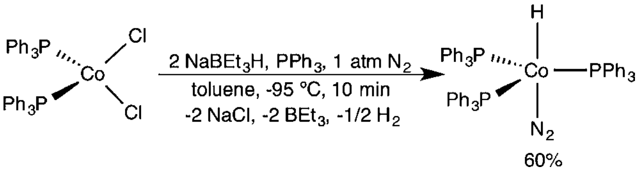
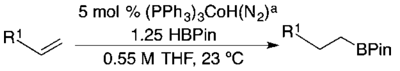
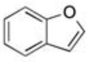
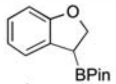
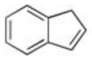
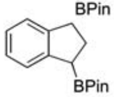
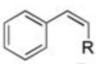
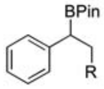
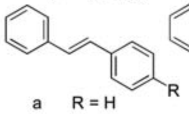
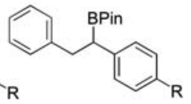
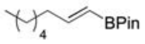
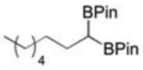
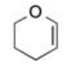
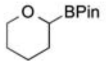


Table 1. Catalytic Alkene Hydroboration Promoted by $(Ph_3P)_3CoH(N_2)$



entry	substrate	major product	isolated yield (%)	time (h)[b]
1			84	2
2			83	1
3				
	a R = H		85 (20:1)[c]	1
	b R = Me		80	0.5
4				
	a R = H		91	1
	b R = OMe		67 (1.6:1)[c]	1.3
5			78	2
6			54	5

[a] Reaction conditions: 0.028 mmol of [Co], 1 mL of THF, 0.55 mmol of substrate, 0.55 mmol of cyclooctane internal standard, and 0.69 mmol of HBPin. [b] Reactions were monitored by GC, and the time noted is the time to >98% conversion. [c] Ratios represent the relative amounts of isomeric hydroboration products as determined by ^1H NMR integration.

The scope of $(PPh_3)_3CoH(N_2)$ promoted alkene hydroboration was evaluated. Each catalytic reaction was conducted with a 0.55 M THF solution of the alkene and 1.25 equiv of HBPin at 23 °C. The results of these studies are reported in Table 1. As with benzofuran, the hydroboration of indene is selective for the benzylic position (entry 2). Styrene (entry 3) and *cis*-*β*-methylstyrene also underwent selective hydroboration with high activity, as complete conversion was observed in 1.0 h and 0.5 h, respectively. Stilbene and 4-methoxystilbene (entry 4) were also effective substrates with the latter exhibiting a slight preference, 1.6:1 for carbon−boron bond formation at the benzylic position adjacent to the more electron-deficient arene. With 1-octenylpinacolborane (entry 5), selective formation of the 1,1-diboron product was observed. Dihydropyran (entry 6) underwent hydroboration with regiochemistry opposite of what is observed using BH_3.[22] In all cases, good to high isolated yields were obtained, and separation of the product from the catalyst residue was readily accomplished by passage through silica.

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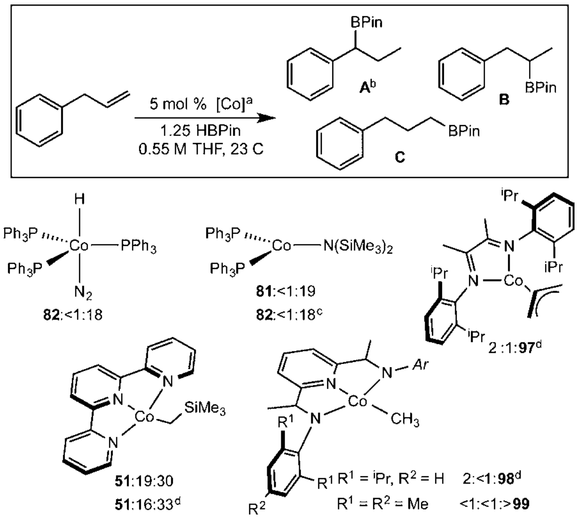
To explore the generality of this method further, the cobalt-catalyzed hydroboration of allylbenzene with HBPin was explored. With 5 mol % of $(Ph_3P)_3CoH(N_2)$, complete conversion to a 83:17 mixture of products was observed with the major product identified as 1-phenylpropylpinacolborane (**A**, Scheme 4). The minor product, 3-phenylpropylpinacolborane (**C**), arises from C−B bond formation at the alkyl terminus.

Scheme 4. Hydroboration of Allylbenzene with HBPin Using Various Cobalt Precursors



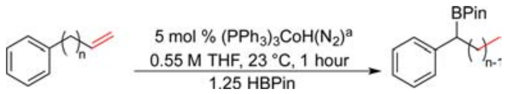
[a] Reaction conditions: 0.028 mmol of [Co], 1 mL of THF, 0.55 mmol of allylbenzene, 0.55 mmol of cyclooctane, and 0.69 mmol of HBPin. [Co] was added last. [b] After the reactions attained >98% conversion, relative ratio of **A**:**B**:**C** determined from GC integration and normalized to 100. Response factors were not determined; however, their ratio is constant. [c] With 5 mol % of PPh_3 added. [d] With 1.5 equiv of HBPin.

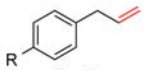
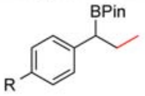
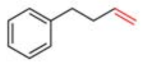
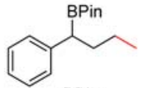
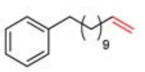
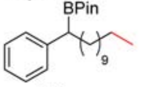
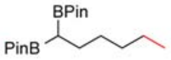
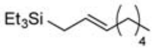
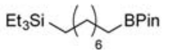
While cobalt-catalyzed alkene isomerization−hydroboration is now well precedented, most catalysts favor products arising from terminal carbon−boron bond formation. With precious metals, only the rhodium-catalyzed reaction of allylbenzene with $BH_3\cdot$THF favors branched products.[23] The unusual preference for benzylic carbon−boron bond formation in allylbenzene hydroboration with HBPin and by $(Ph_3P)_3CoH(N_2)$ prompted comparison with other cobalt precatalysts to gauge how the supporting ligand impacts the selectivity of the reaction, information that will ultimately prove useful in future catalyst design.

As presented in Scheme 4, the branched selectivity for the hydroboration of allylbenzene in the presence of 5 mol % of $(PPh_3)_2CoN(SiMe_3)_2$, a compound reported by Fout and co-workers in the context of catalytic C−N cross coupling,[24] was indistinguishable from $(PPh_3)_3CoH(N_2)$, demonstrating the ratio of phosphine to cobalt does not influence selectivity. In contrast, cobalt compounds bearing sterically demanding, aryl-substituted, and redox-active α-diimine and bis(imino)pyridine chelates yielded 3-phenylpropylpinacolborane (**C**) as the major product with high selectivity, highlighting the preference of these catalysts for forming carbon−boron bonds at terminal positions. With $(terpy)CoCH_2SiMe_3$ (terpy = terpyridine), a mixture of products was obtained with a slight preference for benzylic C−B bond formation over the terminal position.

Because $(PPh_3)_3CoH(N_2)$ is a known alkene isomerization catalyst,[18,21] a protocol was devised to synthesize benzylic organoboronate esters selectively via tandem isomerization−hydroboration. The general procedure involved premixing the alkene and cobalt precursor for 1 h in THF prior to the addition of HBPin. As reported in Table 2, this method is effective for a family of alkenyl arenes with generally high selectivity for the benzylic product. Complete conversion and good to high isolated yields were obtained. Isomerization over a 12-carbon chain (entry 3) highlights the scope of the method, although a longer premixing time of 5 h was required for optimal selectivity. Boronate esters (entry 4) also favored isomerization and provided a route to valuable 1,1-diboron compounds from readily available α,ω-dienes.[25] The unique role of aryl and boronate ester functional groups in promoting the isomerization is highlighted by entry 5, where cobalt-catalyzed hydroboration of the allylsilane produced exclusive terminal selectivity.

Table 2. Catalytic Alkene Isomerization−Hydroboration with HBpin and 5 mol % of $(Ph_3P)_3CoH(N_2)$



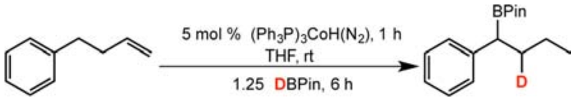
entry	substrate	major product	isolated yield (%)^b	time (h)^b	B:L ratio^c
1					
a R = H			75	1	> 25:1
b R = F			87	0.2	> 25:1
c R = OMe			81	1	10:1
2			82	6	>20:1
3^d			61	24	6:1
4			76	1	8:1:1^e
5			53	19	n/a^f

[a] Reaction conditions: 0.028 mmol of $(PPh_3)_3CoH(N_2)$, 1 mL of THF, 0.55 mmol of benzofuran, 0.55 mmol of cyclooctane. HBPin (0.69 mmol) was added after 1 h. [b] Reactions were monitored by GC, and the time noted is the time to >98% conversion. [c] Ratios represent the relative amounts of isomerization−hydroboration product shown and the isomer with boron incorporated at the terminal position of the alkyl chain. The ratios were determined by ^{1}H NMR integration. [d] Stirred for 5 h prior to HBPin addition. [e] Hexylpinacolborane was also identified in the isolated product. [f] No other isomers were isolated.

To explore the selectivity of cobalt-catalyzed hydroboration following alkene isomerization, a deuterium labeling study was conducted. Addition of DBPin to 4-phenyl-1-butene following 1 h of premixing with $(PPh_3)_3CoH(N_2)$ revealed incorporation of the isotopic label exclusively at the position β to the arene ring (Scheme 5). The selective incorporation of the deuterium at this position indicates that C−B bond formation at the benzylic position is faster than isomerization of 1-phenylbutene, formed from 4-phenyl-1-butene during the premixing period, as isomerization would result in deuterium scrambling.

The erosion of selectivity observed in experiments without premixing of the alkene and catalyst demonstrate that for the initially formed terminal cobalt−alkyl, the rates of C−B bond

Scheme 5. Catalytic Isomerization−Hydroboration of 4-Phenyl-1-butene Using DBPin



formation and β-hydride elimination are competitive. The slower isomerization of 1-phenylbutene relative to 4-phenylbutene likely derives from the preferential formation of η^3-benzyl intermediates following alkene insertion into the Co−H, or in the case of boronate ester directed reactions, coordinatin of an oxygen atom. Cobalt complexes with η^3-benzyl ligands have been observed previously,[26] and similar intermediates have been invoked to account for the selectivity for branched products in the rhodium-catalyzed hydroboration of styrene.[27] Formation of an η^3-benzyl cobalt benzyl intermediate is also consistent with the observed catalyst effects reported in Scheme 4. More sterically hindered ligands such as aryl-substituted α-diimine and bis(imino)pyridines favor carbon−boron bond formation from terminal alkyl intermediates even when the starting alkene is in an internal position.

Additional experiments were conducted to gain insight into the nature of the catalytic active cobalt compound and identity of the resting state. Monitoring the catalytic hydroboration of benzofuran with HBPin in THF-d_8 with 10 mol % of $(PPh_3)_3CoH(N_2)$ by ^{1}H and ^{31}P NMR spectroscopies revealed no detectable change to the catalyst precursor over the hydroboration reaction. To establish the potential role of phosphine dissociation, the hydroboration of benzofuran was conducted with a solution containing 0.028 M $(PPh_3)_3CoH(N_2)$ in the presence of variable amounts of added PPh_3. Upon doubling the concentration of added phosphine from 0.11 to 0.22 M, the initial relative rate constants decreased by a factor of 2. The inhibition by added phosphine, in conjunction with observation of $(PPh_3)_3CoH(N_2)$ as the resting state, support PPh_3 dissociation as an entry point into the catalytic cycle.

In summary, mixtures of readily available phosphine ligands and cobalt precursors are effective for catalytic carbon−boron bond-forming reactions. In the case of PPh_3, $(PPh_3)_3CoH(N_2)$ is effective for alkene hydroboration with nonterminal selectivity offering a route to benzylic boronate esters from a variety of alkenes or 1,1-diboron compounds from α,ω-dienes.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Complete experimental procedures, characterization data for all new compounds, and crystallographic data in CIF format. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b01135.

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Notes

The authors declare no competing financial interest.

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