

Iron-Catalyzed, Atom-Economical, Chemo- and Regioselective Alkene Hydroboration with Pinacolborane**

Lei Zhang, Dongjie Peng, Xuebing Leng, and Zheng Huang*

Dedicated to Professor Maurice Brookhart on the occasion of his 70th birthday

Alkylboronic acid derivatives are now widely used as intermediates in organic synthesis.^[1] For example, Suzuki–Miyaura reactions can efficiently couple C(sp³) organoboron species with aryl and alkyl halides.^[2] An advantage of alkylboronic acid derivatives over other common C(sp³) organometallic nucleophiles is their unique stability: many of them can be readily isolated, purified, and even stored in air.^[1a] There are several methods for the preparation of alkylboronic acid derivatives. One commonly used method involves the conversion of an alkylhalide into a lithium or Grignard reagent, followed by the reaction of the organometallic reagent with boron compounds.^[3] However, the synthetic value of this method is limited, owing to poor functional-group compatibility and the formation of waste inorganic salts. Recently, Hartwig et al. have developed a Rh-catalyzed direct borylation of alkanes with B₂Pin₂ to form alkylboronate esters, albeit under relatively harsh reaction conditions.^[4] More recently, Liu, Marder, Steel, and co-workers reported a convenient approach for the synthesis of alkylboronate esters through Cu-catalyzed borylation of alkyl halides.^[5] However, the method requires the use of an excess of B₂Pin₂ as the borylation reagent, and waste inorganic salts were also generated.

Alternatively, alkylboronic acid derivatives can be prepared by Rh- or Ir-catalyzed alkene hydroborations.^[1b,6] Although dialkylboranes add readily to alkenes, dialkoxyboranes react sluggishly with alkenes in the absence of catalyst. Metal-catalyzed alkene hydroboration is a synthetically useful method, because the reaction is highly atom economical and typically occurs under mild conditions. For example, the Wilkinson catalyst has been extensively used for the hydroboration of a wide range of alkenes.^[6b–o] Unfortunately, side reactions such as dehydrogenative borylation and alkene hydrogenation, can compete with alkene hydroboration.^[1b,6n,7] Another drawback is the low regioselectivity in the hydroboration of vinylarenes, especially with pinacolborane.^[6g,j,k] Moreover, the catalytic performance of the Wilkin-

son complex is extremely sensitive to impurities and the reaction should be handled with extra care.^[6l–n] In many cases relatively high loadings of expensive Rh and Ir catalysts were necessary for good conversion.^[6g,l,n]

The low abundance, high cost, and environmental concerns over precious metals has motivated the investigation of earth-abundant and inexpensive base-metal alternatives in recent years.^[8] Well-defined iron complexes have received tremendous attention over the past decade in the field of homogeneous catalysis.^[9] Recently, Ritter et al. presented an iminopyridine iron catalyst for selective 1,4-hydroboration of 1,3-dienes.^[10] However, to date the hydroboration of widely available and commercially relevant alkenes using iron catalyst has remained unknown. Herein, we report the synthesis of an electron-rich iron pincer complex and its application to the first example of iron-catalyzed alkene hydroborations. This system exhibits unprecedented high efficiency for selective α -olefin hydroborations using pinacolborane.

We commenced our studies by examining the known iron complexes for catalytic hydroboration of 4-methyl-1-pentene **1a** (2 equiv) with pinacolborane (HBPIn). The results are summarized in Table 1. The Ritter complex (iminopyridine)-FeCl₂ **3** acts as a catalyst precursor for 1,3-diene hydroboration.^[10] However, complex **3** (5 mol %), upon addition of NaBHET₃ (15 mol %), did not effect α -olefin hydroboration (entry 1).^[11] The reaction using FeCl₂ alone (5 mol %) or a combination of FeCl₂/2,2'-bipyridine (5 mol % each) in the presence of NaBHET₃ also gave no hydroboration product (entries 2 and 3). Furthermore, iron complex **4**, which contains a bidentate PN ligand (see Table 1), was prepared (see Supporting Information). The reaction using **4** (5 mol %) as the precatalyst in THF at 25 °C gave the anti-Markovnikov hydroboration product **2a** in 5% yield after one hour (entry 4). Iron complexes of tridentate terpyridine and bis(imino)pyridine ligands have been successfully applied to alkene hydrogenation^[12] and hydrosilylation.^[12,13] Encouragingly, the reactions using (terpy)FeCl₂ **5** (5 mol %) and (iPrPDI)FeCl₂ **6** (5 mol %) afforded **2a** in 9 and 61% yields, respectively (entries 5 and 6).

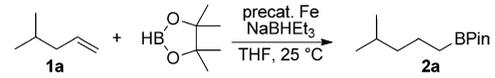
The above data suggest that the use of a tridentate ligands is essential for iron-catalyzed alkene hydroboration. We envisioned that catalyst development for this transformation would benefit from the use of a tridentate electron-donating phosphine ligand. Such a ligand would induce a less electrophilic iron center and may allow easy access to an olefin-ligated Fe^{II} boryl hydride species, which is a potential key intermediate in catalytic alkene hydroboration.^[14] To this end,

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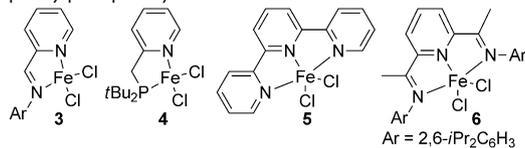
Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201210347>.

Table 1: Iron-catalyzed hydroboration of **1a** with HBPIn.^[a]

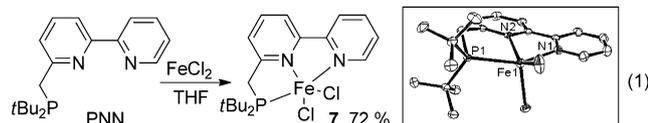


Entry	Precat. ^[b]	NaBHET ₃ [mol %]	t [min]	Yield [%] ^[c]
1	3	15	60	< 2
2	FeCl ₂	15	60	< 2
3	FeCl ₂ /bpy	15	60	< 2
4	4	15	60	5
5	5	15	60	9
6	6	15	60	61
7	7	15	60	> 99
8	7 ^[d]	0.75	10	99
9	none	15	60	0
10	7	0	60	0
11	[Rh(PPh ₃) ₃ Cl]	0	60	68 ^[e]
12	[[Ir(cod)Cl] ₂]/dppe	0	60	75

[a] Reaction conditions: HBPIn (0.5 mmol) and **1a** (1 mmol) in THF (2 mL) at 25 °C. [b] Unless otherwise specified, 5 mol% of pre-catalyst was used. [c] Unless otherwise specified, yields of **2a** were determined by GC analysis using an internal standard. [d] 0.25 mol% of pre-catalyst was used. [e] Dehydrogenative borylation product (18%) was also observed. Yield was determined by ¹H NMR spectroscopy using an internal standard. Bpy = bipyridine, cod = 1,5-cyclooctadiene, dppe = 1,2-bis(diphenylphosphino)ethane.



we sought to develop an electron-rich iron complex with good thermostability by using a bipyridyl-based phosphine ligand (PNN).



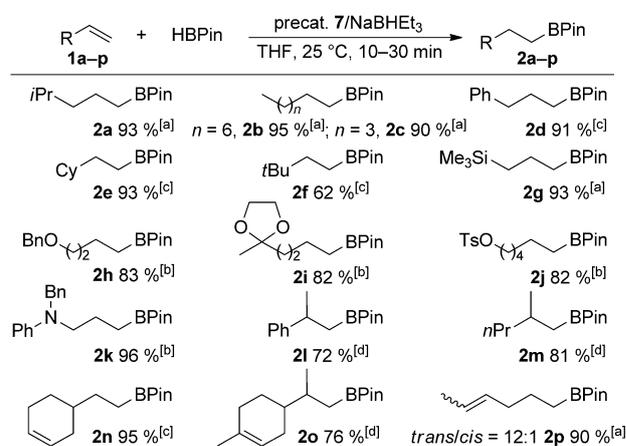
Treatment of the Milstein PNN ligand bearing phosphino-*tert*-butyl groups^[15] with FeCl₂ in THF afforded iron pincer complex **7** in 72% yield [Eq. (1)]. The complex was characterized by ¹H NMR spectroscopy, elemental analysis, and single crystal X-ray diffraction. The solid structure of **7** reveals a distorted square pyramidal geometry around the metal center (see the Supporting Information).

Complex **7** was then tested as the pre-catalyst for alkene hydroboration. Gratifyingly, the reaction of **1a** with HBPIn catalyzed by **7** (5 mol%) upon addition of NaBHET₃ (15 mol%) in THF at 25 °C gave the anti-Markovnikov hydroboration product **2a** in quantitative yield in one hour (Table 1, entry 7). The system is so active that the amount of the pre-catalyst could be reduced to 0.25 mol% and the reaction still afforded 99% of **2a** in 10 min (entry 8). No branched or dehydrogenative borylation products were detected by GC/MS and ¹H NMR analysis. A control experi-

ment without the pre-catalyst **7**, but with NaBHET₃, gave no product **2a** (entry 9). The addition of NaBHET₃ was necessary for catalysis (entry 10).

As a comparison, hydroboration of **1a** with the Wilkinson catalyst, [Rh(PPh₃)₃Cl] (5 mol%), gave **2a** in only 68% yield after one hour (entry 11).^[6g,k,16] Notably, the dehydrogenative borylation product (18%) was also detected by ¹H NMR and GC/MS analysis. Finally, a combination of [[Ir(cod)Cl]₂]/dppe (5 mol% of Ir and dppe; cod = 1,5-cyclooctadiene, dppe = 1,2-bis(diphenylphosphino)ethane) gave **2a** in 75% yield after one hour (entry 12).^[6g] These results indicate that the PNN iron pincer complex is more efficient than the well-known Rh and Ir catalysts for α -olefin hydroboration with HBPIn.

To evaluate the scope of the iron-catalyzed alkene hydroboration, the reactions of a variety of alkenes with HBPIn were carried out using complex **7** as the pre-catalyst (Scheme 1). All reactions were selective for anti-Markovnikov hydroboration. The alkylboronate ester products are



Scheme 1. Iron-catalyzed hydroboration of alkenes (**1a–p**) with HBPIn. Yields shown are of isolated products. Reaction conditions: HBPIn (0.5 mmol) and alkenes **1a–p** (1 mmol) in THF (2 mL) at 25 °C. [a] With **7** (0.25 mol%) and NaBHET₃ (0.75 mol%), 10 min. [b] With **7** (1 mol%) and NaBHET₃ (3 mol%), 30 min. [c] With **7** (2 mol%) and NaBHET₃ (6 mol%), 30 min. [d] With **7** (5 mol%) and NaBHET₃ (15 mol%), 30 min. Bn = benzyl, Cy = cyclohexyl, Pin = pinacol, Ts = *p*-toluenesulfonyl.

moisture- and air-stable, and can be readily purified by flash chromatography. Hydroborations of simple acyclic α -olefins **1a–c** (2 equiv)^[17] with HBPIn occurred within 10 min and formed products **2a–c** in 90–95% yields of isolated products. The substrates γ -phenylpropene (**2d**, 91%) and cyclohexylethene (**2e**, 93%) underwent hydroboration in useful yields. The hydroboration of the sterically demanding *tert*-butylethene afforded the product **2f** in relatively low yield (62%). The iron catalytic system is compatible with alkenes bearing various functional groups. Hydroborations of **1g–k** with HBPIn afforded alkylpinacolboronates containing silyl (**2g**, 93%), ether (**2h**, 83%), acetal (**2i**, 82%), tosylate (**2j**, 82%), and amine (**2k**, 96%) functional groups. Furthermore, 1,1-disubstituted α -olefins, such as α -methylstyrene **1l** and 2-

methyl-1-pentene **1m**, were hydroborated to give **21** and **2m** in 72 and 81 % isolated yields, respectively.

Notably, the PNN iron pincer system is inactive for hydroboration of internal alkenes, such as *trans*-3-octene and cyclooctene. The sensitivity of this catalytic system to steric effects enables the chemoselective hydroboration of a terminal alkene within a molecule containing multiple C=C bonds. For example, the hydroboration of the terminal olefin proceeded without hydroboration of the internal olefin in 4-vinyl-cyclohexene **1n**, to produce 95 % yield of isolated **2n**. The selective hydroboration of 1,1-disubstituted olefin in (\pm)-limonene afforded 76 % yield of isolated **2o**. Moreover, the reaction of 1,4-hexadiene **1p** (*trans/cis* = 12:1) gave 90 % yield of isolated **2p** (*trans/cis* = 12:1) without hydroboration or isomerization of the disubstituted olefin.

The iron-catalyzed chemoselective hydroboration of an α -olefin relative to 1,2-disubstituted olefin is remarkable. As a comparison, [Rh(PPh₃)₃Cl]-catalyzed (5 mol %) hydroboration of **1n** afforded six hydroboration products after one hour, including **2n** (51 %) and the products arising from internal olefin hydroboration (14 % total by-product yield; see the Supporting Information for product distributions). Furthermore, hydroboration of 1,4-hexadiene **1p** (*trans/cis* = 12:1) catalyzed by [Rh(PPh₃)₃Cl] (5 mol %) gave *trans*-**2p** in only 5 % yield after one hour (10 % conversion of HBPIn), together with multiple other hydroboration products. After 15 h, at least six hydroboration products, including *trans*-**2p** (51 %), were detected by GC/MS (see the Supporting Information). We attribute the poor chemoselectivity of the Rh-catalyzed alkene hydroboration to facile internal olefin hydroboration and olefin isomerization.

In contrast to the exclusive formation of hydroboration products in the reactions of alkene substrates **1a–p**, iron-catalyzed hydroboration of styrene **8a** (2 equiv) with HBPIn in THF not only formed the linear hydroboration product **9a** (34 % yield), but also the dehydrogenative borylation product **10a** in 65 % yield after 30 min. Ethylbenzene **11a** (21 % yield relative to HBPIn) formed by styrene hydrogenation was also obtained. It should be noted that dehydrogenative borylation is a common side reaction accompanying metal-catalyzed vinylarene hydroboration with HBPIn.^[6k,7a,18]

The selectivity of iron-catalyzed styrene hydroboration appeared to be solvent sensitive. With toluene as the solvent, the yield of the hydroboration product **9a** (51 %) was somewhat improved versus the reaction in THF (34 %), but the reaction still gave a moderate amount of **10a** (45 %) and **11a** (20 %) (Table 2). Similarly, reactions of 4-methylstyrene (**8b**), 4-methoxystyrene (**8c**), and 4-fluorostyrene (**8d**) with HBPIn in toluene gave a mixture of linear hydroboration products **9b–d**, dehydrogenative borylation products **10b–d**, and hydrogenation products **11b–d** (Table 2). No side product resulting from dehydrogenative borylation was detected when using acetonitrile as the solvent, although the reaction of styrene with HBPIn gave the hydroboration product **9a** in only 5 % yield after 30 min.^[19]

We speculated that acetonitrile plays a role in inhibiting both the alkene hydroboration and dehydrogenative borylation processes, but the suppressing effect of acetonitrile on the latter is more significant. Indeed, in the presence of acetonitrile

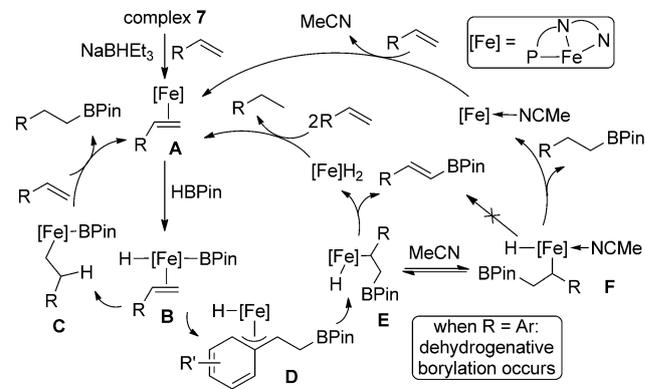
Table 2: Iron-catalyzed hydroboration of vinylarenes (**8a–d**) with HBPIn.^[a]

Entry	R	9/10/11 ^[b]		
		(no MeCN)	(20 mol % MeCN)	(40 mol % MeCN)
1	H, 8a	51:45:20	86:–:–	78:–:–
2	Me, 8b	52:41:21	95:–:–	83:–:–
3	MeO, 8c	51:43:29	80:5:–	88:–:–
4	F, 8d	39:55:17	82:10:–	81:–:–

[a] Reaction conditions: HBPIn (0.5 mmol) and **8a–8d** (1 mmol) in toluene (2 mL) with complex **7** (2 mol %) and NaBHET₃ (6 mol %) at 25 °C for 30 min. [b] Data shown are yields [%] relative to HBPIn, and were determined by ¹H NMR spectroscopy using an internal standard.

trile (20 mol %), reactions of styrene and 4-methylstyrene with HBPIn in toluene exclusively formed linear boronate esters **9a** (86 %) and **9b** (95 %) after 30 min (Table 2, entries 1 and 2), whereas reactions of 4-methoxystyrene and 4-fluorostyrene gave linear boronate esters as the major products (80 and 82 %, respectively) with the formation of a small amount of vinylboronate esters (5 and 10 %). To our delight, doubling the amount of acetonitrile (40 mol % relative to HBPIn) resulted in the exclusive formation of the addition products **9c** (88 %) and **9d** (81 %; Table 2, entries 3 and 4).

On the basis of our preliminary data and precedent regarding related iron-catalyzed alkene addition processes, we propose the mechanism of iron-catalyzed alkene hydroborations shown in Scheme 2. Following the coordination of



Scheme 2. Proposed mechanism for the iron-catalyzed alkene hydroboration and dehydrogenative borylation reactions.

alkene to the iron center, oxidative addition of HBPIn to **A** forms the formal 18 electron Fe^{II} boryl hydride species **B**, which is similar to those believed to be involved in alkene hydrogenation and hydrosilylation, and in 1,3-diene hydroboration and hydrosilylation catalyzed by iron complexes.^[14] Terminal alkenes, except for vinylarenes, undergo selective 1,2-insertion into the Fe–H bond to form linear alkyl complex **C**.^[6l,o] Reductive elimination then generates the anti-Markovnikov product.

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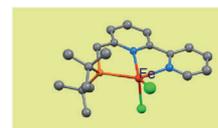
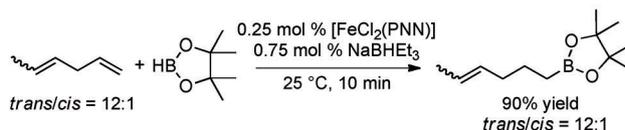
Communications



Organometallic Catalysis

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Iron-Catalyzed, Atom-Economical,
Chemo- and Regioselective Alkene
Hydroboration with Pinacolborane



$[\text{FeCl}_2(\text{PNN})]$

Precious iron: A new PNN iron complex has been developed for use in an iron-catalyzed alkene hydroboration reaction under mild conditions. The environmentally friendly and earth-abundant iron

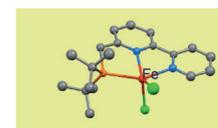
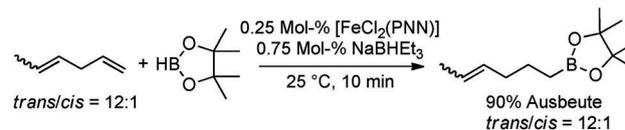
catalyst system is superior to precious-metal systems in terms of efficiency and selectivity for α -olefin hydroborations with pinacolborane.



Organometallkatalyse

L. Zhang, D. Peng, X. Leng,
Z. Huang*

Iron-Catalyzed, Atom-Economical,
Chemo- and Regioselective Alkene
Hydroboration with Pinacolborane



$[\text{FeCl}_2(\text{PNN})]$

Edles Eisen: Ein Eisenkomplex mit P,N,N-Ligand für katalytische Alkenhydroborierungen unter milden Bedingungen wurde entwickelt. Das System mit dem umweltverträglichen und leicht

verfügbaren Katalysatormetall ist Edelmetallsystemen bei α -Olefin-Hydroborierungen mit Pinakolboran hinsichtlich Effizienz und Selektivität überlegen.

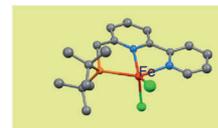
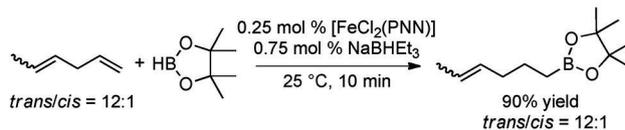
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Organometallic Catalysis

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Precious iron: A new PNN iron complex has been developed for use in an iron-catalyzed alkene hydroboration reaction under mild conditions. The environmentally friendly and earth-abundant iron

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