COMMUNICATION

Iron catalyzed hydroboration: unlocking reactivity through ligand modulation

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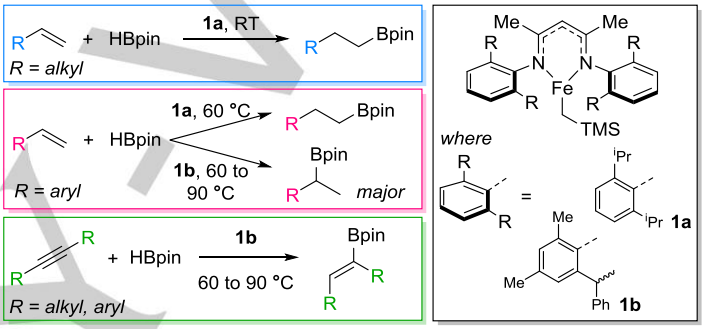
Abstract: Iron catalyzed hydroboration of alkenes and alkynes is reported. A simple change in ligand structure leads to a remarkable and extensive change in catalyst activity. Reactions proceed efficiently over a wide range of challenging substrates including activated, unactivated and sterically encumbered motifs. Conditions are mild and do not require the use of reducing agents or other additives. Large excesses of borating reagent are not required, allowing for exquisite control of chemo- and regioselectivity in the presence of multiple double bonds. Mechanistic insight reveals that the reaction is likely to proceed *via* a highly reactive iron hydride intermediate.

Hydroboration is the addition of a B–H bond across an unsaturated moiety and is a valuable transformation in the synthesis of alkyl borane building blocks for use in organic synthesis,[1] not least in Suzuki-Miyaura cross-coupling.[2] The use of pinacol- or catecholborane as a source of B–H dominates the literature due to the stability of the resulting products. Many are air stable, can be isolated, purified and stored on the bench for many months. However, the relative inertness of these boranes renders them essentially unreactive towards unsaturated bonds and catalysis is necessary under moderate to forcing conditions. It is also important to note that historically precious metals have been used for catalytic HB,[1, 3] but due to the high cost, toxicity and low earth abundance of these metals, there has been renewed interest in the discovery of catalysts containing earth-abundant, non-toxic, first row transition metals.[4] In the recent literature, elegant examples have been presented using iron pre-catalysts.[5]

One of the most common methods to undertake HB using iron catalysis is to use a neutral ligand in the presence of FeX_2 (where X = Cl, Br, OAc and the pre-catalyst is prepared *in situ* or used as a ligated complex) and a catalytic amount of Grignard reagent or hydride additive.[6] Previously, we have exploited iron pre-catalysts that are capable of undergoing redox neutral, σ-bond metathesis type reactivity,[7] avoiding the need for activation by a Grignard or other reducing agent and we were intrigued by their potential to undergo catalytic HB. β-Diketiminate ligands have shown exceptional reactivity when used in conjunction with a host of main group elements and transition metals,[8] but the power of this ligand in iron catalysis is vastly underexplored.[7b, 9] Benefits of the β-diketiminate ligand in iron catalysis include the simplicity, modular tunability and cost-effectiveness which complements the rationale behind base metal catalysis. We herein report the use of two iron(II) β-diketiminate complexes for the HB of both simple and more challenging alkenes along with alkynes (Scheme 1). The catalyst system described does not need exogenous reductant (activation is facile) and therefore, with so few species present in solution, Reaction Progress Kinetic Analysis[10] can also be used to rapidly gain mechanistic insight.



Scheme 1. Fe(II) pre-catalysts used to catalyze the HB of alkenes and alkynes.

We initiated our studies using pre-catalyst **1a** which contains the classical 2,6-diisopropyl motif.[11] Pleasingly, not only do traditional HB substrates, such as 1-hexene, 1-octene and allyl benzene, undergo catalysis at room temperature (forming **2a**, **2b** and **2c** respectively in 100% spectroscopic yield, Figure 1), but more complex substrates such as 1,2-epoxy-5-hexene can be functionalized but not to the detriment of the epoxide (**2d**).[12] Likewise, a primary phosphinoalkene (**2o**) does not undergo competing coordination/deactivation or intramolecular hydrofunctionalization, instead HB operates exclusively. Substrates obtained from renewable resources also undergo facile HB. For example in the presence of two equivalents of HBpin isoprene, myrcene and β-farnesene with their multiple double bonds are selectively hydroborated at the terminal positions (**2g**, **2h**, **2i**). Limonene and valencene only undergo HB at the exocyclic double bond (**2j**, **2l**). Note the use of one equivalent of borane per double bond: it is not necessary to manipulate stoichiometries and use a vast excess of olefin in order to obtain a favorable result with these complex systems, indeed the benefit of these substrates lies in the retention of multiple double bonds in the molecule, making them suitable for further functionalization. This level of chemoselectivity is rare in the field of iron catalysis; reactions of complementary selectivity have only been reported by Ritter and Huang.[5a, e, f] In this latter report, the authors also clearly demonstrate the comparably poor selectivity of Wilkinson's catalyst in diene HB, highlighting the benefits of iron catalysis.

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Unfortunately, with our iron catalysis, compounds containing ketones, for example nootkatone, show competing boration of the carbonyl and the desired product, **2k**, could not be isolated. The chemistry is also extended to HB using catecholborane (**2a'**, **2c'**, **2e'**) where good isolated yield can be achieved using inert atmosphere handling conditions.

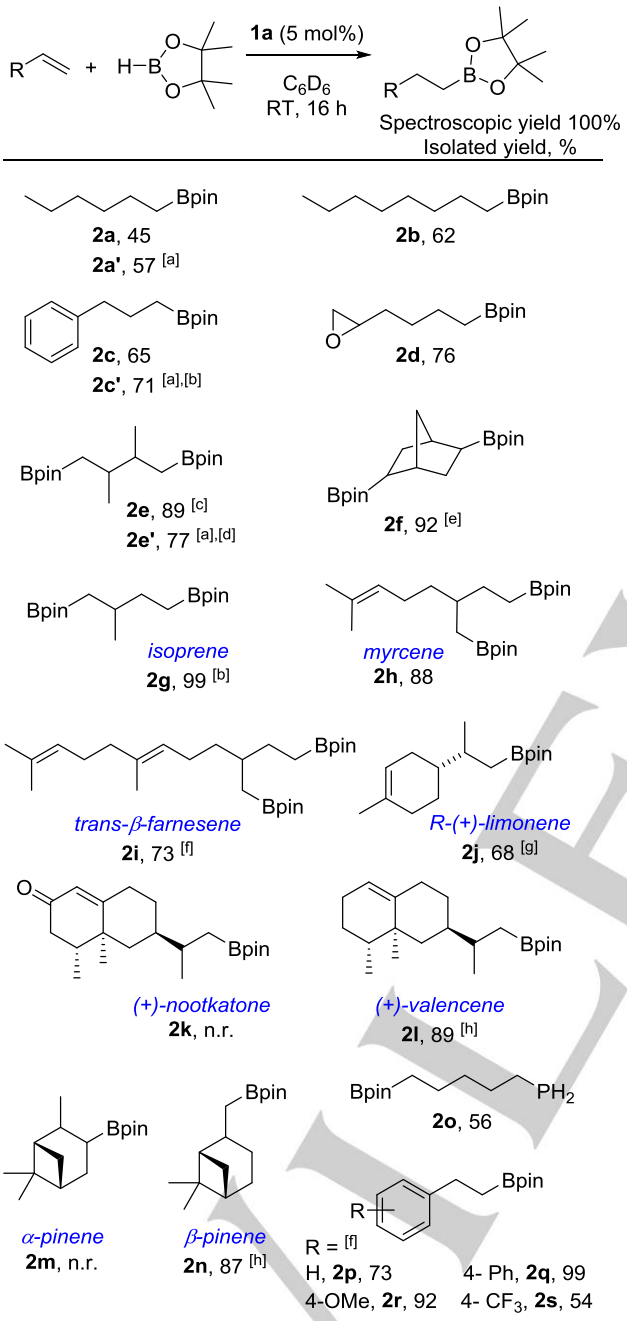
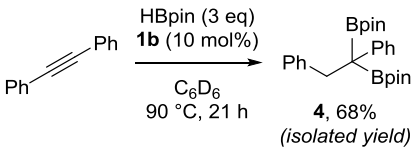


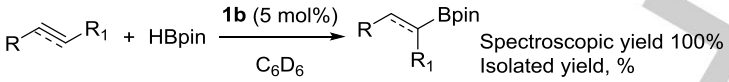
Figure 1: Substrate scope for the HB of simple alkenes. All reactions performed using 0.5 mmol alkene (0.25 mmol for dienes) and 0.5 mmol HBpin, 100% spectroscopic yield obtained in all cases except n.r. = desired reaction was not achieved. [a] Reaction performed with 0.5 mmol HBcat. [b] 60 °C, 7 h. [c] 36 h. [d] 90 °C, 2.5 h. [e] 60 °C, 48 h, mixture of 2,5- & 2,6-HB isomers (1:1). [f] 10 mol% **1a**, 60 °C, 16 h. [g] 24 h. [h] 60 °C, 16 h.

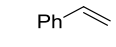
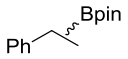
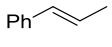
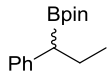
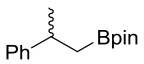
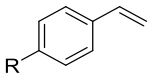
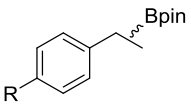
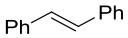
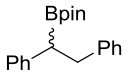
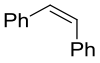
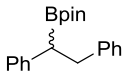
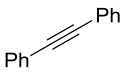
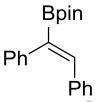
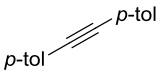
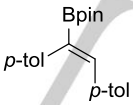
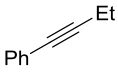
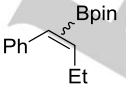
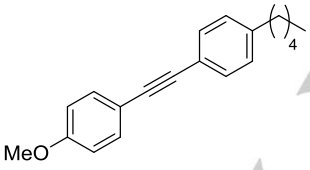
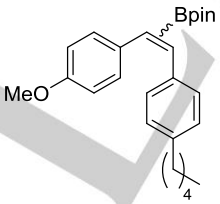
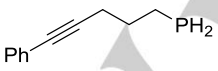
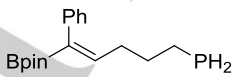
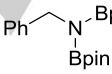
When other more challenging substrates are tackled, higher temperatures are necessary. Heating styrene to 60 °C is needed to achieve 100% spectroscopic yield of **2p**: the rate of reaction at room temperature is around 45 times slower than that obtained for 1-hexene.[13] 4-Ph, 4-OMe and 4-CF_3 styrene also give exclusive formation of the anti-Markovnikov product (**2q**, **2r**, **2s**). Again, anti-Markovnikov selectivity is rare irrespective of choice of metal catalyst,[14] but not least in iron catalysis[5e] where many examples rely on a blocking group in the α-position[5b, g] to prevent Markovnikov selectivity,[5h] or only anti-Markovnikov reactivity with an unsubstituted styrene has been provided.[5d, k] Encouraged by these result under heating, we moved to explore the reactivity of α- and β-methyl styrene. Using **1a**, β-methylstyrene isomerizes to give allylbenzene, which then reacts with HBpin affording **2c**.[14b, d, 15] We therefore sought to develop a new iron β-diketiminate complex that has enhanced electronic and steric properties which may proffer more favorable reactivity than the simple 2,6-diisopropyl substituted system. Inspired by Coates' use of *sec*-phenylethyl substituted diimine pre-catalysts, which showed enhanced tacticity, regiocontrol and reduced chain-walking in olefin polymerizations,[16] we developed a second generation iron β-diketiminate pre-catalyst (**1b**, Scheme 1).[17] When **1b** catalyzes the HB of styrene, only 3 h are necessary to give a comparable yield of HB product, but remarkably, this subtle change in ligand structure gives a vast change in regioselectivity: good levels of Markovnikov selectivity are obtained (**3a**, Table 1, Entry 1). This trend is mirrored in the other styrenes tested (Entries 4 to 6). Importantly, dehydrogenative HB and hydrogenation are not observed during the HB of styrene. α- and β-methyl styrene (Entries 2 and 3) can be functionalized in good isolated yield when the reaction is performed with heating. Internal activated double bonds also react; *cis*-stilbene gives 75% yield **3g** after 16 h at 60 °C, whereas *trans*-stilbene yields 75% **3g** after only 5 h at 70 °C (Entries 7 and 8). Diphenylacetylene reacts to give the *Z* product, **3h**, exclusively (Entry 9). To our delight double HB of diphenylacetylene generates the unique 1,1-dipinacolborane product (**4**) after heating to 90 °C (Scheme 2).[18]



Scheme 2: Double HB of diphenylacetylene yields the 1,1-diborated product.

Table 1: Vinyl arene and alkyne substrate scope in iron-catalyzed HB, catalyzed by **1b**.



Entry	Alkene	Product		Temp., time	Isolated yield (%) [a]
1			**3a** **3a'** [b]	60 °C, 3 h 60 °C, 2.5 h	92 (65 M:35 AM) 77 (65 M:35 AM)
2			**3b**	90 °C, 3 h	84
3			**3c**	60 °C, 3 h 60 °C, 18 h [c]	98 48
4 5 6			**3d**, R = Ph **3e**, R = OMe **3f**, R = CF_3	60 °C, 18 h 60 °C, 4 h 90 °C, 3 h	78 (7 M:3 AM) 81 (3 M:2 AM) 71 (7 M:3 AM)
7			**3g**	70 °C, 5 h	75
8			**3g**	60 °C, 16 h	75
9			**3h** **3h'** [b]	90 °C, 6 h 90 °C, 3.5 h	86 98
10			**3i**	90 °C, 2.5 h	95
11			**3j**	90 °C, 3 h	99 (85:15)
12			**3k**	90 °C, 3 h	97 (1:1)
13			**3l**	60 °C, 16 h	79
14 [d]			**3m**	90 °C, 16 h	84

Conditions: 0.5 mmol alkene, 0.5 mmol HBpin, 5 mol% [Fe], 0.4 mL C_6D_6. [a] Isolated yield obtained by silica gel chromatography (100% spectroscopic yield obtained in all cases except Entry 14). M = Markovnikov; AM = anti-Markovnikov. [b] Reaction carried out with 0.5 mmol HBcat. [c] Reaction using **1a** (5 mol%), 100% spectroscopic yield. [d] Not isolated, 0.25 mmol benzonitrile.

Other internal alkynes also react to give the *Z*-alkene product exclusively, heteroatoms are tolerated and high levels of regioselectivity are obtained (Table 1, Entries 10 to 13). Unfortunately, catalytic reactivity is not observed with terminal alkynes such as phenylacetylene, but in contrast benzonitrile reacts with two equivalents of HBpin to give the *N*,*N*-diborated benzylamine (Table 1, Entry 14).

Returning to the aliphatic substrates reported in Figure 1, use of **1b** also allows for an improvement in reactivity compared to that obtained with **1a** (Table 2). This enhanced reactivity is acutely

observed for 2,3-butadiene, valencene and β-pinene (Entries 1, 3, 4) where the reactions are between five and eight times faster. Remarkably, although α-pinene shows no reactivity with **1a**, 80% conversion is observed after 16 h at 90 °C with **1b,** however, this occurs with concomitant isomerization to form **2n**, a reaction previously only reported by Chirik using cobalt catalysis.[14d]

Table 2: Improved reaction conditions and yields of aliphatic substrates are also obtained when **1b** is employed as a pre-catalyst.

Entry	Product	Conditions to obtain 100% spectroscopic yield	
		1a (5 mol%)	**1b** (5 mol%)
1	**2e**	RT, 36 h	RT, 7 h
2	**2g**	60 °C, 7 h	60 °C, 2.5 h
3	**2l**	60 °C, 16 h	60 °C, 2 h
4	**2n**	60 °C, 16 h	60 °C, 2.5 h
5	**2p**	RT, 16 h	RT, 16 h

Conditions: 5 mol% **1a** or **1b**, 0.4 mL C_6D_6. Spectroscopic yield obtained by $^{11}B\{^1H\}$ NMR (complete consumption of HBpin observed along with the formation of one new product peak).

The lack of catalytic reactivity with phenylacetylene hints at reaction mechanism. On addition of phenylacetylene to the pre-catalyst, the reaction mixture immediately changes from yellow to red, indicative of the formation of an iron-acetylene complex,[19] which does not undergo HB. This result is intuitive as the acidic proton of phenylacetylene results in loss of $Si(CH_3)_4$ whereas HBpin is more likely to furnish $BpinCH_2TMS$ (**5**) and an iron hydride. A stoichiometric reaction of **1a** and HBpin results in the formation of **5** which is confirmed by mass spectrometry and NMR analysis. **5** can also be observed in the reaction when 1-hexene is added. Once the iron hydride is formed it is able to react with an olefin and then subsequent boration with HBpin (or HBcat) releases **2a** and regenerates the iron hydride.[13] Unfortunately the hydride could not be detected by ^1H NMR, but this is not inconceivable; three coordinate iron hydrides are incredibly reactive and their isolation or even detection is not trivial.[20] Although we have already shown that catalyst initiation for such transformations is likely to be radical mediated,[7b] addition of radical trap (iodomethyl)cyclopropane, to the reaction of 1-hexene, HBpin and 5 mol% **1a** after 30 minutes (16% product formed) results in reaction quenching. To support our proposed reaction mechanism Reaction Progress Kinetic Analysis studies were undertaken.[10] No catalyst deactivation or product inhibition is detected and the reaction is determined to be first order in **1a**, HBpin and 1-hexene,[13] thus supporting our postulated mechanism.

In summary, we have developed a new catalytic system for the HB of alkenes using HBpin and HBcat that does not need exogenous reducing agents or activators and can be undertaken with a strict 1:1 ratio of reagents. The chemistry has been extended beyond classical substrates and includes natural products, vinyl arenes and alkynes. RPKA demonstrates that the reaction is first order in substrates and catalyst, and stoichiometric studies provide evidence for a catalytic cycle that is likely to proceed *via* an iron hydride. Reactivity of styrenes demonstrates that a subtle change in ligand structure can lead to a vast change in regioselectivity, whilst alkynes show much improved reactivity with this change in pre-catalyst. Double HB of diphenylacetylene is possible and gives the geminal dipinacolborane product.

Acknowledgements

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Keywords: iron • homogeneous catalysis • hydroboration • alkenes • alkynes

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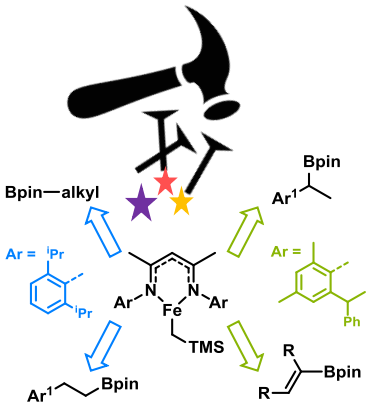

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