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Iron-Catalyzed 1,4-Hydroboration of 1,3-Dienes

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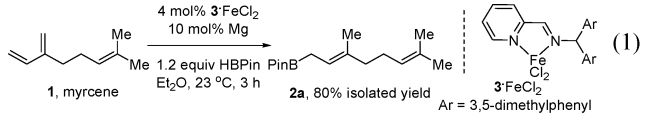
Iron can adopt formal oxidation states ranging from −II[1] to +VI.[2] Iron complexes are used as catalysts in synthetic chemistry for carbon−heteroatom[3] and carbon−carbon bond-forming reactions.[4] Low-valent iron complexes can catalyze cross-coupling,[4] cycloisomerization,[5] and cycloaddition reactions.[6,7] We are interested in iron catalysis for the identification of useful, previously inaccessible reaction chemistry and report here C−B bond formation by hydroboration of 1,3-dienes. To our knowledge, there are no other examples of Fe-catalyzed hydroboration reactions of olefinic substrates. The allylborane products are formed regio- and stereoselectively with (*E*)-double bond geometry exclusively and are challenging to access selectively with conventional chemistry.

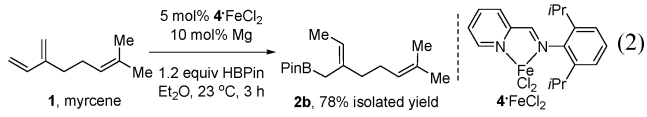
We have previously reported a 1,4-addition reaction of α-olefins to dienes using an iminopyridine−ferrous chloride complex[8] with magnesium metal as an in situ reducing agent.[9] In this communication, we describe the use of analogous, readily prepared iminopyridine-derived iron complexes as catalysts for the regioselective 1,4-addition of pinacolborane (HBPin) to substituted 1,3-dienes (eq 1).

Allylboranes are versatile intermediates employed in oxidation to form allylic alcohols,[10] allylation to give homoallylic alcohols[11] and amines,[12] and Suzuki cross-coupling reactions.[13] Traditional methods for synthesizing allylboranes involve basic main-group organometallics, such as Grignard and organolithium reagents, that are incompatible with electrophilic functional groups.[11a] While transition-metal-catalyzed hydroboration of olefins has been studied extensively with great success,[14] hydroboration of dienes to access allylboranes is less-established. Pd(0) catalyzes the 1,4-addition of catecholborane to unfunctionalized 1,3-dienes such as 1,3-pentadiene and isoprene to give (*Z*)-branched allylboranes,[15] while Ni^{II}-[16] and Rh^{I}-catalyzed[17] reactions are selective for 1,2-addition.

The synthesis of linear (*E*)-γ-disubstituted allylboranes is attractive because, for example, they can afford trisubstituted allylic alcohols stereospecifically and add to electrophiles to generate quaternary stereocenters with control of diastereoselectivity. Challenges in the synthesis of linear (*E*)-γ-disubstituted allylboranes via hydroboration of 1,3-dienes include control of chemoselectivity to favor 1,4- over 1,2-addition, control of regioselectivity to favor C−B bond formation at a single diene terminus, and control of stereoselectivity to favor (*E*)-olefin geometry. The hydroboration reaction presented herein controls all three types of selectivity. A general method for synthesizing linear (*E*)-γ-disubstituted allylboranes has not been reported previously.[18]

We observed that hydroboration of myrcene (**1**) catalyzed by the iminopyridine−iron(II) complex **3**·$FeCl_2$ upon addition of magnesium metal afforded geranylpinacolborane (**2a**) in 80% yield after 3 h at 23 °C (eq 1). The combination of ligand, ferrous chloride, and magnesium was necessary for catalysis. Pinacolborane generally afforded allylboranes that were stable toward air, water, and chromatography on silica gel; other borolanes, such as those derived from catecholborane, were not stable toward hydrolysis or chromatography on silica gel.[19]





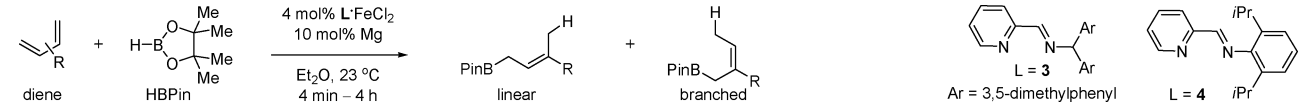
Evaluation of different bidentate ligands (see the Supporting Information) showed that iminopyridine ligands gave the highest yields for hydroboration. The redox activity of iminopyridine ligands may play a role in effecting efficient catalysis.[20] Ligand optimization revealed that variation of the substituent of the imine nitrogen modulates the 1,4-regioselectivity to favor either the branched or linear isomer (eqs 1 and 2). 1,4-Addition of pinacolborane to myrcene (**1**) catalyzed by **3**·$FeCl_2$ produced geranylpinacolborane (**2a**) with 93:7 (**2a/2b**) regioselectivity and >99:1 *E*/*Z* selectivity in 89% overall yield (eq 1). When catalyst **4**·$FeCl_2$ was used, the regioselectivity was inverted, and branched allylborane **2b** was obtained as the major product in 78% isolated yield (92% yield of combined regioisomers; eq 2). The ligand-controlled regioselectivity is of synthetic value and may be set during migratory insertion (see the mechanistic hypothesis shown in Scheme 1).

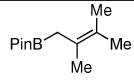
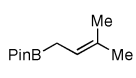
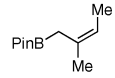
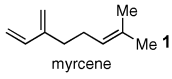
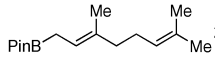
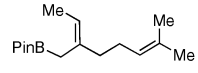
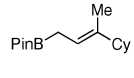
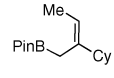
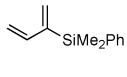
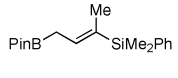
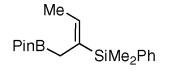
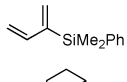
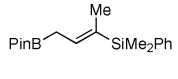
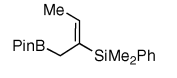
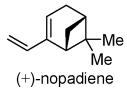
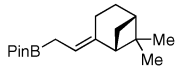
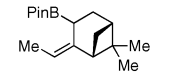
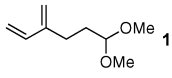
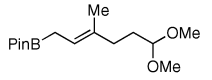
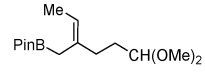
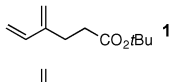
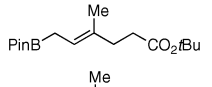
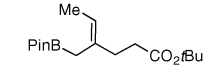
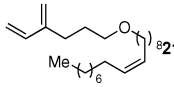
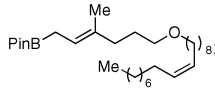
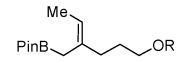
Hydroboration of various 1,3-dienes occurred within 4 min to 4 h, depending on the substrate and ligand, and proceeded equally efficiently with commodity (98%) and high-purity (99.998%) ferrous chloride as the iron source. As shown in Table 1,[21] the regioselectivity for 1,4-hydroboration of 2-substituted dienes increased as the size of the 2-substituent increased: isoprene afforded prenylboronate ester **10a** with 90:10 regioselectivity; geranylborane **2a** was obtained with 93:7 regioselectivity; and 2-cyclohexylbutadiene (**11**) and 2-dimethyl(phenyl)silylbutadiene (**13**) were hydroborated with regioselectivities of 94:6 and 99:1, respectively. The regioselectivity of 1,4-addition to **13** could be inverted from 99:1 to <1:99 by using the iron complex **4**·$FeCl_2$, which differs from iron complex **3**·$FeCl_2$ only in the iminopyridine substituent (entries 6, 7). Both of the allylboranes **14a** and **14b** are difficult to synthesize otherwise: silaboration of allenes yields 2-borylallylsilanes.[22] In addition to 2-substituted dienes, 2,3-disubstituted diene **5** participated in Fe-catalyzed hydroboration to regioselectively give allylborane **6**. The 1,4-disubstituted diene **7** was hydroborated efficiently to give allylborane **8**. Hydroboration of the 1,2-disubstituted diene (+)-nopadiene (**15**) gave C−B bond formation at the less-substituted diene terminus with 98:2 regioselectivity.[23]

The Fe-catalyzed hydroboration can be performed in the presence of electrophilic functionality, such as the ester in **19**, which is incompatible with the basic conditions of traditional allylborane syntheses.[11a] Notably, the hydroboration is chemoselective, and 1,4-addition to 1,3-dienes proceeds without hydroboration of isolated

10.1021/ja9048493 CCC: $40.75

Table 1. Substrate Scope for Fe-Catalyzed 1,4-Hydroboration of 1,3-Dienes

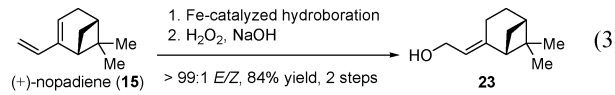


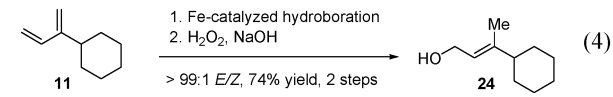
Entry	Diene		Linear Product		Branched Product		L	(Linear: Branched)	*E*:*Z* (major)	Yield
1		**5**		**6**	--		**4**[a]	--	--	91%
2		**7**		**8**	--		**4**[a]	--	--	83%[b]
3	 isoprene	**9**		**10a**		**10b**	**3**	90:10	--	92%[c]
4	 myrcene	**1**		**2a**		**2b**	**3**	93:7	> 99:1	89%
5		**11**		**12a**		**12b**	**3**	94:6	> 99:1	68%[b,d]
6		**13**		**14a**		**14b**	**3**	99:1	> 99:1	91%[b]
7		**13**		**14a**		**14b**	**4**[a]	< 1:99	> 99:1	73%[b]
8	 (+)-nopadiene	**15**		**16a**		**16b**	**3**	98:2	> 99:1	91%[b]
9		**17**		**18a**		**18b**	**3**	94:6	> 99:1	71%[b]
10		**19**		**20a**		**20b**	**3**	94:6	> 99:1	66%[b,d]
11		**21**		**22a**		**22b**	**3**	93:7	> 99:1	68%[b,d]

[a] Using 5 mol % **4**·$FeCl_2$. [b] Using 15 mol % 2,3-dimethyl-1,3-butadiene as an additive.[21] [c] Using 1.5 equiv of HBPin. [d] Product degradation was observed upon purification by chromatography on silica gel; the yield can be higher if used in situ. See, for example, eq 3.

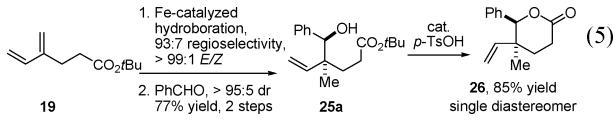
olefins such as in **21**. We attribute the high chemoselectivity of diene versus olefin hydroboration to the affinity of 1,3-dienes for low-valent iron.[24] The Fe-catalyzed hydroboration of every diene investigated was selective for 1,4-addition to produce the allylborane stereo- and regioselectively. 1,2-Addition products could not be detected by ^{1}H NMR analysis. The major regioisomers **12a**−**22a** were formed with (*E*)-double bond geometry exclusively, consistent with the mechanism proposed in Scheme 1. Products with trisubstituted double bonds can otherwise be challenging to synthesize stereoselectively, especially when the substituents have similar sizes.[25]

Allylic alcohols with trisubstituted double bonds are substrates for asymmetric catalytic reactions, such as Noyori hydrogenation,[26] isomerization to generate chiral aldehydes,[27] and Sharpless asymmetric epoxidation.[28] All of these reactions require the alcohol substrate to be stereochemically pure with respect to double bond geometry in order to attain high levels of enantioselectivity. The Fe-catalyzed hydroboration presented here provides ready access to allylic alcohols with (*E*)-trisubstituted double bonds in high stereoselectivity (>99:1; eqs 3 and 4).[25] For example, allylic alcohol **23** was synthesized in two steps by hydroboration of (+)-nopadiene (**15**) followed by oxidation to provide only the (*E*)-isomer **23** in 84% yield over two steps.



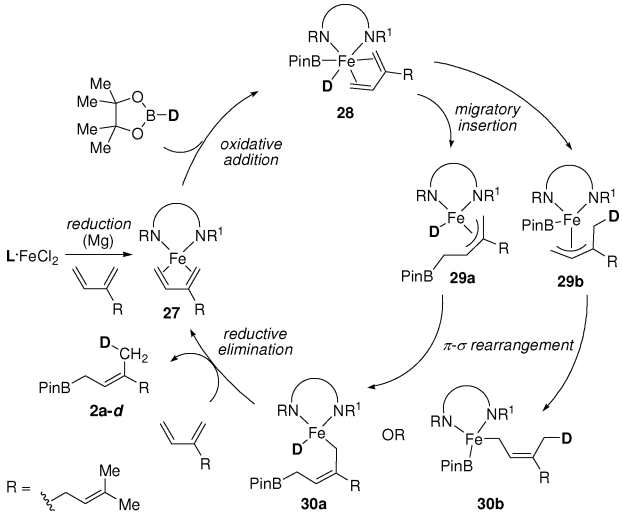


The Fe-catalyzed reaction can also be used in a one-pot hydroboration−allylation reaction, as shown in eq 5. Addition of benzaldehyde subsequent to 1,4-hydroboration of ester **19** gave a 93:7 mixture of homoallylic alcohols **25a** and **25b** resulting from the two regioisomers **20a** and **20b**. Homoallylic alcohol **25a** was formed as a single diastereomer, as determined by ^{1}H NMR spectroscopy. Lactone formation afforded **26** in 85% yield as a single diastereomer. Alcohol **25a** and δ-lactone **26** both contain an all-carbon quaternary center; the relative stereochemistry in **25a** and **26** is a result of the *E* configuration of the γ-disubstituted allylborane generated in the Fe-catalyzed hydroboration.



A preliminary mechanistic analysis led us to propose the catalytic cycle shown in Scheme 1. The deuterium atom from pinacolborane-d_1 was found at the methyl group of the hydroborated product **2a-*d*** exclusively. Selective deuteration is consistent with migratory insertion into either the Fe−B or Fe−H bond via the allyliron intermediate **29a** or **29b**, respectively, but cannot distinguish between the two pathways. The proposed compounds **29a** and **29b** were not observed during catalysis. The turnover-limiting step and the reversibility of the steps of the catalytic cycle are currently unknown and, hence, the ligand-controlled regioselectivity (e.g., entries 6 vs 7) could be determined during oxidative addition or migratory insertion. When the branched isomer **2b** was subjected to the reaction conditions of hydroboration, no linear isomer **2a** was observed, which established that at least one of the steps following the regioselectivity-determining step is irreversible. The selectivity for double bond geometry can be rationalized by the proposed mechanism via syn migratory insertion to Fe−allyl **29a** or **29b**.

Scheme 1. Proposed Mechanism for 1,4-Hydroboration



In conclusion, we have reported a chemo-, regio-, and stereoselective Fe-catalyzed hydroboration of 1,3-dienes to afford linear (*E*)-γ-disubstituted allylboranes. The iminopyridine−Fe-catalyzed reaction provides access to allylboranes—versatile building blocks—that are challenging to prepare by traditional allylborane syntheses or other known transition-metal-catalyzed reactions. The hydroboration reaction demonstrates previously unknown reactivity for iron.

Acknowledgment. We thank Novartis for a fellowship for J.Y.W., Materia for a generous donation of Grubbs II catalyst, and the ACS PRF.

Supporting Information Available: Detailed experimental procedures and spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(1) (a) Jonas, K.; Schieferstein, L.; Krüger, C.; Tsay, Y. H. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 550–551. (b) Ellis, J. E. *Organometallics* **2003**, *22*, 3322–3338. (c) Fürstner, A.; Krause, H.; Lehmann, C. W. *Angew. Chem., Int. Ed.* **2006**, *45*, 440–444.
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