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

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

Jessica Y. Wu, Benoît Moreau and Tobias Ritter*

Department of Chemistry and Chemical Biology, Harvard University, 12 Oxford Street, Cambridge, MA

RECEIVED DATE; ritter@chemistry.harvard.edu

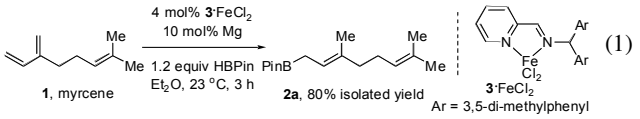
Iron can adopt formal oxidation states ranging from –II[1] to +VI.[2] Iron complexes are used as catalysts in synthetic chemistry for carbon–heteroatom[3] and carbon–carbon bond forming reactions.[4] Low-valent iron complexes can catalyze cross-coupling,[4] cycloisomerization,[5] and cycloaddition reactions.[6,7] 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[8] complex 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).

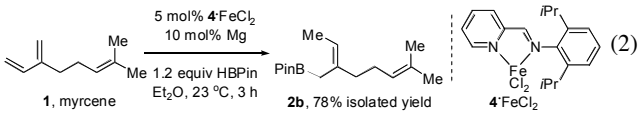
Allylboranes are versatile intermediates employed in oxidation to allylic alcohols,[10] allylation to give homoallylic alcohols[11] and amines,[12] and Suzuki cross-coupling reactions.[13] Traditional methods to synthesize allylboranes involve basic main group organometallics, such as Grignard and organolithium 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. Palladium(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] and 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 to synthesize linear (*E*)-γ-disubstituted allylboranes has not been reported previously.[18]

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



(1)

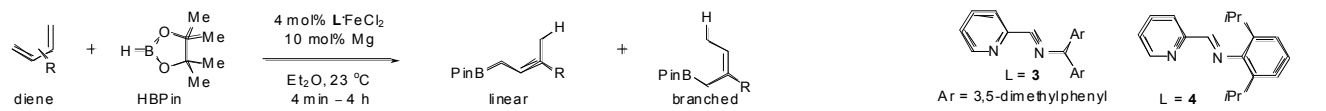


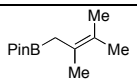
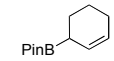
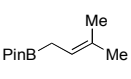
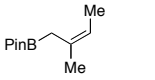
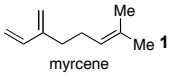
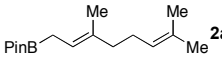
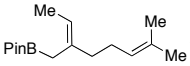
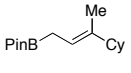
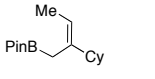
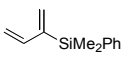
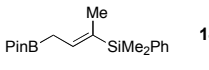
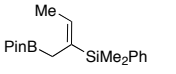
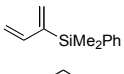
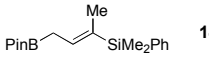
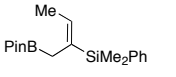
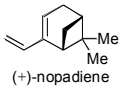
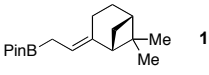
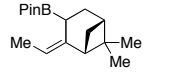
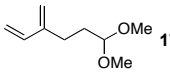
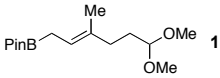
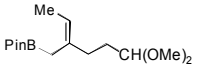
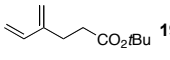
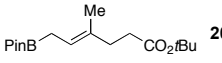
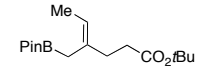
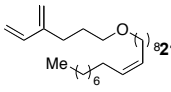
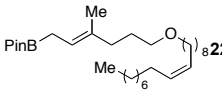
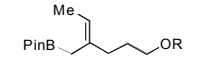
(2)

Evaluation of different bidentate ligands (see 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 the linear isomer (eqs 1 and 2). 1,4-Addition of pinacolborane to myrcene (**1**) catalyzed by **3**·$FeCl_2$ produced geranylpinacolborane (**2a**) in 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 inverted to afford branched allylborane **2b** 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 mechanistic hypothesis, Scheme 1).

Hydroboration of various 1,3-dienes occurred within 4 min to 4 h, depending on the substrate and ligand, and proceeds as efficiently with commodity ferrous chloride (98% purity) as with high-purity ferrous chloride (99.998% purity) as 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 in 93:7 regioselectivity; 2-cyclohexylbutadiene (**11**) and 2-dimethylphenylsilylbutadiene (**13**) were hydroborated in 94:6 and 99:1 regioselectivity, 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 only in the iminopyridine substituent from iron complex **3**·$FeCl_2$ (entries 6, 7). Both 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]

Table 1. Substrate scope for Fe-catalyzed 1,4-hydroboration of 1,3-dienes.

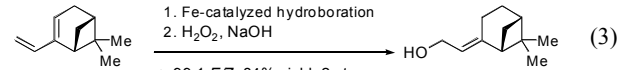


Entry	Diene		Linear Product		Branched Product		L	(Linear: Branched)	*E*:*Z* (major)	Yield
1		**5**		**6**	--		**4**[a]	--	--	91%
2		**7**		**8**	--		**4**[a]	--	--	83%[b]
3	 isoprene	**9**		**10a**		**10b**	**3**	90:10	--	92%[c]
4	 myrcene	**1**		**2a**		**2b**	**3**	93:7	> 99:1	89%
5		**11**		**12a**		**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]

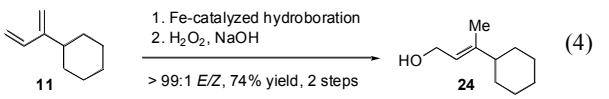
a) 5 mol% **4**·$FeCl_2$ was used. b) 15 mol% 2,3-dimethyl-1,3-butadiene was used as an additive.[21] c) 1.5 equiv HBPin was used. d) Product degradation was observed upon purification by chromatography on silica gel; yield can be higher if used in situ. See, for example, eq 4.

The Fe-catalyzed hydroboration can be performed in the presence of electrophilic functionality, such as the ester in **19**, that is incompatible with the basic conditions of traditional allylborane syntheses.[11a] Notably, hydroboration is chemoselective, and 1,4-addition to 1,3-dienes proceeds without hydroboration of isolated 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 all dienes investigated is selective for 1,4-addition to produce allylboranes stereo- and regioselectively. 1,2-Addition products could not be detected by ^{1}H NMR. The major regioisomers **12a**–**22a** were formed with (*E*)-double bond geometry exclusively, consistent with the proposed mechanism in Scheme 1. Products with trisubstituted double bonds can otherwise be challenging to synthesize stereoselectively, especially when the substituents are similar in size.[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 reactions require the alcohol substrate to be stereochemically pure with respect to double bond geometry to attain high levels of enantioselectivity. The presented Fe-catalyzed hydroboration 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 *E*-isomer **23** in 84% yield over 2 steps.



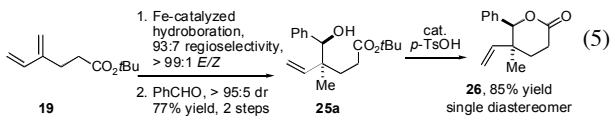
(3)



(4)

The Fe-catalyzed reaction can also be used in a one-pot hydroboration-allylation reaction, as shown in eq 5. Benzaldehyde was added, subsequent to 1,4-hydroboration of ester **19**, to give 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*-

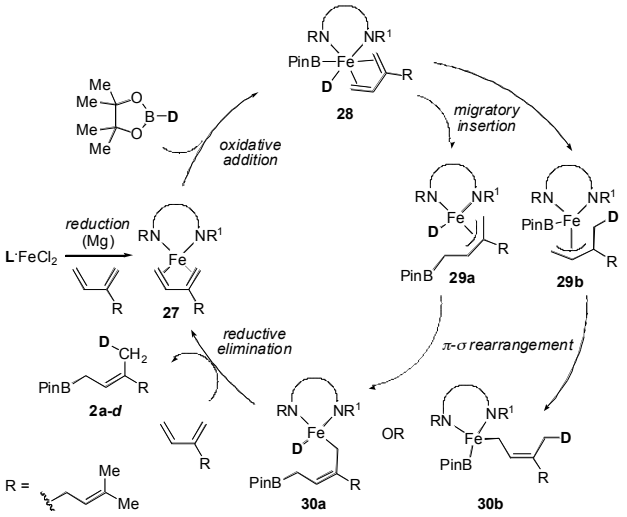
configuration of the γ-disubstituted allylborane generated in the Fe-catalyzed hydroboration.



(5)

A preliminary mechanistic analysis led us to propose the catalytic cycle shown in Scheme 1. The deuterium atom from pinacolborane-*d* 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 the Fe–H bond via the iron allyl intermediates **29a** and **29b**, respectively but cannot distinguish between the two pathways. 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 step after the regioselectivity-determining step is irreversible. The selectivity for double bond geometry can be rationalized by the proposed mechanism due to *syn* migratory insertion to Fe-allyl **29a** or **29b**.

Scheme 1. Proposed mechanism for 1,4-hydroboration.



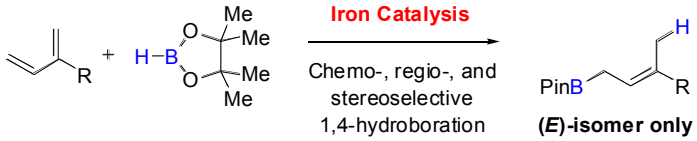
In conclusion, we report a chemo-, regio-, and stereoselective Fe-catalyzed hydroboration of 1,3-dienes to afford linear (*E*)-γ-disubstituted allylboranes. The iminopyridine-Fe-catalyzed reaction provides access to allylboranes—versatile building blocks—that are challenging to prepare by traditional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

Acknowledgement. We thank Novartis for a fellowship for JYW, 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.

REFERENCES

(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.
(2) Berry, J. F.; Bill, E.; Bothe, E.; George, S. D.; Mienert, B.; Neese, F.; Wieghardt, K. *Science* **2006**, *312*, 1937–1941.
(3) (a) Barton, D. H. R.; Gastiger, M. J.; Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1983**, *1*, 41–43. (b) Chen, M. S.; White, M. C. *Science* **2007**, *318*, 783–787.
(4) For reviews, see: (a) Leitner, A. Iron-catalyzed Cross-coupling Reactions. In *Iron Catalysis in Organic Chemistry*; Plietker, B., Ed.; Wiley-VCH: Weinheim, 2008; pp 147–176. (b) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500–1511. (c) Fürstner, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 1364–1367.
(5) (a) Takacs, J. M.; Anderson, L. G.; Madhavan, G. V. B.; Creswell, M. W.; Seely, F. L.; Devroy, W. F. *Organometallics* **1986**, *5*, 2395–2398. (b) Fürstner, A.; Martin, R.; Majima, K. *J. Am. Chem. Soc.* **2005**, *127*, 12236–12237. (c) Fürstner, A.; Majima, K.; Martin, R.; Krause, H.; Kattnig, E.; Goddard, R.; Lehmann, C. W. *J. Am. Chem. Soc.* **2008**, *130*, 1992–2004.
(6) For examples, see: (a) tom Dieck, H.; Dietrich, J. *Chemische Berichte-Recueil* **1984**, *117*, 694–701. (b) tom Dieck, H.; Dietrich, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 781–783. (c) Bouwkamp, M. W.; Bowman, A. C.; Lobkovsky, E.; Chirik, P. J. *J. Am. Chem. Soc.* **2006**, *128*, 13340–13341.
(7) For reviews, see: (a) Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217–6254. (b) Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3317–3321. (c) Correa, A.; Mancheño, O. G.; Bolm, C. *Chem. Soc. Rev.* **2008**, *37*, 1108–1117. (d) *Iron Catalysis in Organic Chemistry*; Plietker, B., Ed.; Wiley-VCH: Weinheim, 2008.
(8) Similar iminopyridine-$FeCl_2$ complexes have been reported: Gibson, V. C.; O'Reilly, R. K.; Wass, D. F.; White, A. J. P.; Williams, D. J. *Dalton Trans.* **2003**, 2824–2830.
(9) Moreau, B.; Wu, J. Y.; Ritter, T. *Org. Lett.* **2009**, *11*, 337–339.
(10) Brown, H. C.; Zaidlewicz, M. In *Organic Syntheses Via Boranes*, *Vol. 2*; Aldrich Chemical Company: Milwaukee, 2001; pp 118–120.
(11) (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293. (b) Bubnov, Y. N. *Pure Appl. Chem.* **1987**, *59*, 895–906. (c) Brown, H. C.; Zaidlewicz, M. In *Organic Syntheses Via Boranes*, *Vol. 2*; Aldrich Chemical Company: Milwaukee, 2001; pp 189–194 and pp 207–216. (d) Kennedy, J. W. J.; Hall, D. G. *Angew. Chem., Int. Ed.* **2003**, *42*, 4732–4739.
(12) For recent examples, see: (a) Sugiura, M.; Hirano, K.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126*, 7182–7183. (b) Solin, N.; Wallner, O. A.; Szabó, K. J. *Org. Lett.* **2005**, *7*, 689–691. (c) Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2007**, *129*, 15398–15404.
(13) Sebelius, S.; Olsson, V. J.; Wallner, O. A.; Szabó, K. J. *J. Am. Chem. Soc.* **2006**, *128*, 8150–8151.
(14) For reviews of transition-metal-catalyzed hydroboration, see: (a) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179–1191. (b) Beletskaya, I.; Pelter, A. *Tetrahedron* **1997**, *53*, 4957–5026.
(15) Satoh, M.; Nomoto, Y.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1989**, *30*, 3789–3792.
(16) Zaidlewicz, M.; Meller, J. *Tetrahedron Lett.* **1997**, *38*, 7279–7282.
(17) Matsumoto, Y.; Hayashi, T. *Tetrahedron Lett.* **1991**, *32*, 3387–3390.
(18) For a Pd-catalyzed synthesis of geranylpinacolborane from geraniol, see: (a) Dutheuil, G.; Selander, N.; Szabó, K. J.; Aggarwal, V. K. *Synthesis* **2008**, *14*, 2293–2297. Pt(0)-catalyzed diboration of isoprene gave a 2:1 isoprene:B_2(Pin)$_2$ adduct: (b) Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun.* **1996**, 2073–2074. For an example of 1,4-diboration of 1,3-dienes to access (*Z*)-allylic diboranes, see: (c) Ballard, C. E.; Morken, J. P. *Synthesis* **2004**, 1321–1324.
(19) Alkylboranes such as 9-BBN and diisopinocampheylborane were ineffective hydroborating agents under the reaction conditions shown in eqs 1 and 2.
(20) Lu, C.; Bill, E.; Weyhermüller, T.; Bothe, E.; Wieghardt, K. *J. Am. Chem. Soc.* **2008**, *130*, 3181–3197.
(21) 2,3-Dimethyl-1,3-butadiene was used as an additive to stabilize low-valent iron generated from reduction of the ferrous chloride complex.
(22) Suginome, M.; Ohmori, Y.; Ito, Y. *J. Organomet. Chem.* **2000**, *611*, 403–413.
(23) For Fe-catalyzed hydroboration of the 1-substituted diene 1,3-decadiene, see Supporting Information.
(24) Knölker, H. J. *Chem. Soc. Rev.* **1999**, *28*, 151–157.
(25) (a) Yu, J. S.; Kleckley, T. S.; Wiemer, D. F. *Org. Lett.* **2005**, *7*, 4803–4806. (b) Bissada, S.; Lau, C. K.; Bernstein, M. A.; Dufresne, C. *Can. J. Chem.* **1994**, *72*, 1866–1869. (c) Bellucci, C.; Gualtieri, F.; Scapecchi, S.; Teodori, E.; Budriesi, R.; Chiarini, A. *Il Farmaco* **1989**, *44*, 1167–1191. (d) For a stereoselective synthesis of trisubstituted allylic alcohols, see: Langille, N. F.; Jamison, T. F. *Org. Lett.* **2006**, *8*, 3761–3764.
(26) Takaya, H.; Ohta, T.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Inoue, S.; Kasahara, I.; Noyori, R. *J. Am. Chem. Soc.* **1987**, *109*, 1596–1597.
(27) Tanaka, K.; Qiao, S.; Tobisu, M.; Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 9870–9871.
(28) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974–5976.



A chemo-, regio-, and stereoselective iron-catalyzed 1,4-hydroboration of dienes to synthesize γ-disubstituted allylboranes was developed. 1,4-Hydroboration of 2-substituted dienes forms allylborane products with (*E*)-trisubstituted double bonds exclusively.